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ASSOCIATE TRAINING PROGRAMS IN THE Medical and Biological Sciences at the National Institutes of Health

1972 CATALOG

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NIH ASSOCIATE TRAINING PROGRAMS
1972 Schedule

March 3	Deadline for receipt at NIH of completed applications. (Early commissioning applications are requested by February 1.)
May 8 to 26	Interview period at NIH campus, Bethesda, Maryland. (By invitation only.)
June 12 to 23	Notification to applicants.

BOOK STACKS
DOCUMENTS

FOREWORD

The National Institutes of Health conducts and supports research to find better ways of preventing or curing disease and lengthening life. In pursuit of that mission, NIH provides broad support for biomedical research, research training, and construction of research facilities in the Nation's medical and dental schools, universities, and other research centers. This is the NIH extramural program.

NIH conducts laboratory and clinical research in its own facilities on its 306-acre campus in Bethesda, Md. For example, in the past year, over 4,000 patients were admitted for investigative studies in the Clinical Center—a research hospital with 516 patient beds and 1,100 laboratories. At any point in time, more than 1,400 research projects are in progress here on the Bethesda campus and at field offices directed from here. This is the NIH intramural program.

Of the 2,130 NIH staff members with doctorates, more than 1,000 have M.D. degrees, 862 have Ph. D. degrees, and some have both; 114 have D.D.S. degrees, and 60 have D.V.M. degrees. These individuals with their 3,800 scientifically trained assistants, represent most of the disciplines that contribute to new medical knowledge.

In this scientific community, many opportunities for professional development are available to physicians and others who are undertaking careers in medical or related research, or in academic medicine. The purpose of this catalog is to set forth in one place brief descriptions of programs of concern to those interested in Associateships at the NIH.

Roger L. Black, M.D.
Associate Director
The Clinical Center

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PART ONE

General Characteristics of Associateships

UNUSUAL opportunities for training and experience in clinical and laboratory investigation are available to physicians and dentists who receive appointments as Clinical, Research, and Staff Associates at the National Institutes of Health. These positions provide broad opportunities for career development in most of the health specialties as well as the basic science disciplines.

Appointments to the Associate Training Program are based on intellectual attainment and demonstrated research interest and ability. An individual's background in research is often a decisive factor in making selections. This applies more significantly in certain areas—such as internal medicine and psychiatry—than in others—such as surgery and radiology. Selections are made through a matching process, explained on p. 10.

Each Associate participates in a research program under the direction of his preceptor. Preceptors are staff members who give generously of their time to help the Associate—not only in relation to research problems under investigation, but in any way they can to enrich the experience of the Associate during his stay at NIH. The levels of research responsibility and latitude given to an Associate depend upon his training and experience as well as his interests and initiative.

Separate didactic exercises are designed to complement Clinical and Research Associateships, but Associates in all categories are welcome to attend any of the exercises which can accommodate them if their schedules permit. In addition, postgraduate instruction is available through evening courses offered by the Graduate Program of the Foundation for Advanced Education in the Sciences, Inc. (see Part Four). Associates in many program areas are expected to take advantage of academic opportunities on the NIH campus.

A candidate may enter the Associate Program as a member of the Public Health Service Commissioned Corps, or as a civilian employee. The various methods of entering an Associateship are explained in Part II.

All applicants are carefully considered. To strengthen and expand its potential for continuing effective research, the National Institutes of

Health welcomes applications from interested women and members of all minority groups.

The Clinical Associate

The Clinical Associate participates in both clinical and laboratory research. Institute programs differ in the proportion of time devoted to laboratory and clinical responsibilities.

Ward activities are under immediate supervision of competent clinical investigators, and include a wide variety of rounds, conferences, and other instructive exercises. Proximity to the patient's bedside of collaborating scientists from many biological disciplines has created an unusual opportunity for clinical investigation at the NIH Clinical Center. The environment of the Clinical Center is also enriched by the presence of medical students from country-wide medical schools with whom the Clinical Associate has close association and shares patient care responsibilities.

Clinical Associates are not in formal residency training programs, even though they may be performing many of the same functions that residents do in other hospitals. Some Associates appointed to Dermatology, Neurology, and Psychiatry programs are recommended for a limited amount of residency credit by their respective program chiefs. Associates in positions providing further training in Internal Medicine who remain at NIH for a third year may receive credit for this year upon application to the American Board of Internal Medicine.

The Dental Clinical Associate

Like his physician Clinical Associate counterpart, the Dental Clinical Associate may participate in laboratory and clinical research, while at the same time enhancing his professional skills by providing treatment to the NIH research patient pool serviced by the Dental Services Branch, National Institute of Dental Research.

During the 2-year tenure of the Associateship, full opportunity is provided for: (1) familiarization with all ongoing research programs of relevance to dentistry; (2) affiliation, in a preceptor-preceptee relationship, with one or more program leaders, so as to allow meaningful participation in a mutually acceptable area of investigation; and (3) extension of scientific background through rounds, conferences, seminars and formalized course work.

The Research Associate

The Research Associate devotes the larger portion of his time to laboratory research in the biomedical sciences. His preceptor is responsible for training him in research methodology and design, and for guiding him in the conduct of specific research undertakings and in the interpretation of results. A real effort is made to select research problems which will enable the Associate to gain breadth and perspective, encounter a variety of laboratory problems, and learn many different approaches rather than become a specialist in one or two refined techniques.

In addition, the Research Associate participates in a series of formal tutorial seminars and informal discussion groups designed in content and emphasis for prospective independent investigators. This program is designed to furnish the training in basic medical sciences normally received by Ph.D. candidates but not generally by candidates for the M.D. degree.

The Pharmacology Research Associate

Through an expansion of the NIH Associate Training Program, the National Institutes of Health is increasing its commitment to develop scientific manpower for both basic and applied research in pharmacology and closely related areas of biomedical science.

The Pharmacology Research Associate devotes the larger portion of his time to laboratory research. He receives intensive research training in a number of disciplines related to modern pharmacology. He also attends formal teaching seminars and informal discussion groups which will provide him with the opportunity to master selected topics perhaps not adequately covered during his academic training.

The Staff Associate

The Staff Associate position provides opportunities for those highly qualified candidates who could contribute significantly to research in areas which are not specifically designated in the Research or Clinical Associate categories. The Staff Associate may participate in either laboratory or clinical research or both, depending upon the activities of the

senior investigator with whom he works. Research experience may be supplemented by formal evening study courses, as well as by attendance at lectures by guest speakers and a variety of regularly scheduled seminars.

PART TWO

Applying for an Associateship

Methods of Entering An Associateship:

The following procedures for entering NIH Associate appointments are available to qualified candidates:

PHS Commissioned Corps:

1. PHS CORD Program
2. Active Duty Assignment

Candidate usually applies during the latter part of his senior year in medical school for duty to begin either (A) following one or more years of residency training or (B) immediately after internship.

If selected for an appointment to begin after one or more years of residency training, applicant will be deferred through the PHS CORD Program (see p. 6 for details of this program). Then he serves 2 years as a commissioned officer on active duty at NIH, which satisfies his military obligation.

If candidates prefers to accept a position which will allow him to enter NIH immediately following internship, no deferment is involved and is not needed since he immediately begins to serve his military obligation as a PHS commissioned officer.

Candidate may apply for both of the above types of appointment simultaneously.

With respect to dentists, minimum qualification for appointment is 1 year of accredited internship, or possession of equivalent advanced training beyond the dental degree. Dentists who have recently completed specialty training will be given particular consideration. Selection will usually be made one year prior to the effective date of appointment. Thus, for example, senior dental students who will enter an accredited internship July 1, 1972, are eligible to apply for an appointment commencing in 1973. Dentists are not eligible for the CORD Program.

A candidate's application for a commission in the Public Health Service does not commit him to accept a commission in the event he is not se-

lected for an Associate position at NIH. However, there are many splendid alternative opportunities for physicians and dentists in the Public Health Service which may appeal to such a candidate, and this commission application would be usable for such appointments.

Early Commissioning:

Qualified candidates who will be in their senior or last year of medical school during academic year 1972–73 may apply for an Associateship through this program. Candidate may apply for duty to begin either (A) following one or more years of residency training or (B) immediately after internship. If a year or more of residency training is required by the selecting program, CORD deferment for the necessary year or years will be provided. (For details of the CORD Program see below; for details of Early Commissioning see p. 9.)

Civilian Employment:

Candidates may apply for NIH Associateships and indicate a desire for entrance on duty as a civilian. However, this method of employment will not satisfy a military obligation. Therefore, a civilian appointment is advisable only for those candidates who do not have a service obligation or who are ineligible for the PHS Commissioned Corps or the PHS CORD Program, and/or are willing to take the risk. For the candidate electing to enter through civilian employment, statements relating to the PHS Commissioned Corps, the commissioning process, and the CORD Program would not apply. The specific program selecting the candidate will advise regarding the appropriate employment mechanism, i.e. Civil Service appointment or Staff Fellowship.

Commissioned Officer Residency Deferment Program

The Commissioned Officer Residency Deferment Program (CORD), developed and conducted by the U.S. Public Health Service with the cooperation of the Selective Service System, permits a limited number of draft-eligible physicians (1) to become Inactive Reserve officers in the Commissioned Corps of the Public Health Service and (2) to complete 1 or more years of formal residency training before serving on active duty. Dentists are ineligible for the CORD Program.

CORD Program participants are appointed commissioned officers in the Inactive Reserve of the Public Health Service. They do not receive pay from the Service until called to active duty. The stipend normally paid by the hospital to residents may be accepted by CORD Program officers.

In addition to being fully qualified for active duty in the Commissioned Corps of the Public Health Service, participation in the CORD Program requires that an applicant must:

- Be a citizen of the United States.
- Meet the physical standards of the PHS.
- Satisfactorily complete an internship approved by the Council on Medical Education of the American Medical Association. (However, application will be accepted when internship is an integral part of medical school curriculum or incorporated as part of residency training.)
- Be a graduate of a medical school approved by the Council on Medical Education of the American Medical Association.
- Be liable for 2 years of service under the general provision of the Military Selective Service Act.
- Pursue *clinical* training which is fully creditable toward fulfillment of minimum residency requirements for certification by an American medical specialty board.

When residency training is completed and/or deferment is terminated, the CORD Program officer is obligated to serve on active duty with the Public Health Service for a period of at least 24 months. This period of service will satisfy Selective Service obligations and no further service is required.

It should be noted that, even though tentatively selected for the CORD Program, an applicant cannot participate unless also found fully qualified for appointment as a commissioned officer.

The questions most frequently asked by CORD Program applicants and participants are answered below:

Q. May I apply simultaneously for the Berry and CORD Programs?

A. Yes.

Q. As an intern in a USPHS hospital (or other uniformed service hospital), am I eligible for the CORD Program?

A. If you are interning or have interned as a commissioned officer on active duty in the Army, Navy, Air Force, or Public Health Service, you are not eligible to participate in the CORD Program.

Q. Are participants in the Senior Medical Student Program and Senior ROTC of the Army (or other service) eligible for the CORD Program?

A. No.

Q. Are participating in the Military Services Senior Medical Student Program or Senior ROTC Program eligible for the CORD Program?

A. No.

Q. May I be deferred for a research fellowship?

A. No, CORD Program deferments are granted only for residency training in the clinical and public health specialities.

Q. I have applied for the CORD Program. Will the induction notice I recently received from my local Selective Service Board alter my status as a CORD Program applicant?

A. Yes. If you receive an induction notice after applying for the CORD Program, notify the Office of Personnel, PHS, immediately.

Q. Is there an age limit for the CORD Program?

A. Yes. You must complete CORD Program participation and begin active duty before age 32.

Q. If I am not selected for the NIH Associate Program, may I be considered for deferment under some other PHS activity?

A. Yes. If you apply and are not accepted for an NIH Associate assignment, you may elect (1) to be considered for residency deferment and subsequent active duty in one of the other activities of the Public Health Service, (2) to request active duty, or (3) to withdraw your application for a commission.

Q. I have received notification of selection for CORD Program participation and deferment beginning July 1, 1973. Is it possible for my deferment to begin on February 1?

A. No. Deferment before July 1 cannot be arranged.

Q. I was selected for the CORD Program and residency training in surgery but have now decided I wish to train in pediatrics. May I change my specialty?

A. No. Changes in specialty are not permitted after selections are made.

Q. May I change hospitals while participating in the CORD Program?

A. Yes, provided the new program is approved by the Council on Medical Education of the American Medical Association, all the training is fully creditable by your specialty board, and you notify the Office of Personnel, PHS.

Q. Is it possible to withdraw from the program prior to actual deferment?

A. Yes. You may withdraw your CORD Program application at any time prior to appointment as a commissioned officer, or, if you have already been appointed, you may resign the commission.

Q. May I be deferred for graduate training?

A. No, deferment may not be recommended for periods of basic science or other graduate training unless the academic training is an integral part of a clinical residency program and counts toward satisfying minimum board requirements.

Q. For what rank am I eligible?

A. If you enter the CORD Program immediately following internship, you will be appointed in the grade of Assistant Surgeon (Inactive Reserve), which is equivalent to Lieutenant, jg., in the Navy. When called to active duty, you will receive a promotion to the grade of

Surgeon (Reserve), which is equivalent to Lieutenant Commander in the Navy.

Q. What happens if I am not found qualified for a commission?

A. If you are not found qualified for a commission, you cannot participate in the CORD Program—even though tentatively selected—and you will be so notified as soon as the determination is made.

Q. I am now in residency training. May I apply for the CORD Program?

A. Yes, provided you comply with the application requirements and have not received an induction notice.

Q. Upon completion of my residency training and/or deferment, what is my obligation to the PHS?

A. Two years of active duty satisfies your obligation to the PHS as well as to Selective Service.

Early Commissioning Program for Medical Students (PHS Senior COSTEP Program)

Qualified students who are attending accredited schools of medicine may be appointed and placed on active duty as commissioned officers in the Reserve Corps of the Public Health Service during their senior or final year. They receive full pay and allowances as Junior Assistant Health Service Officers (equivalent to Navy Ensign), plus payment of tuition, fees, and other related expenses. In return for this financial support, they are obligated to serve on active duty as medical officers with the PHS for a minimum of two years.

To be eligible for early commissioning, the student must meet the following requirements of the PHS:

1. Be a citizen of the United States.
2. Meet the medical fitness standards.
3. Be enrolled in good standing in an accredited school of medicine (or osteopathy) in the senior or final year, and have begun formal studies required as part of the curriculum for the senior or final year of medical school on the date of entry on active duty.
4. Agree in writing to serve a minimum of two years with the sponsoring PHS program.

INTERNSHIP

Candidates selected may serve their Internships either within or outside the Public Health Service. Students electing and matched through the National Intern Residency Matching Program with Internships with PHS hospitals will be continued on active duty with the pay and allowances of their rank. (Note: this time does not count toward the obligated service.) Students matched for Internships with other hopsitals will be

placed in an inactive duty status and will receive their pay or stipend from the training hospital. Following internship candidates will usually complete residency training (usually one year for NIH programs) for which they receive deferment through the PHS CORD Program before entering on active duty to serve their two years obligated duty. Some appointments will be made for immediate active duty following internship.

Applications cannot be considered from members of another uniformed service or anyone having other service commitments upon graduation other than to the Public Health Service.

NIH is seeking women candidates with an interest in research. They may enter associateships either as a PHS Commissioned Officer or in a civilian capacity. However, to receive the benefits of the Early Commissioning (Senior COSTEP) Program, *all* candidates must qualify for and accept a commission in the PHS.

Applications cannot be considered from members of another uniformed service or anyone having a service commitment upon graduation other than to the Public Health Service.

Method of Selection—Matching Program

Selections for the Clinical, Research, and Staff Associate appointments are made through a matching process in which the candidate's preferences are matched with the Institute preferences.

In the application packet, a candidate will find several sheets, each headed "Program Area Selection Check List." After reading Part Three of this catalog, he should check off on these sheets the areas in which he is interested. He does not indicate his preferences at this point, and he is not limited to any particular number of choices. The check marks that he makes will determine the laboratories and branches to which his application will be circulated at the National Institutes of Health. Although most appointments are for 1974 or later, with interim deferment for residency training through the CORD Program, the candidate will find some Research or Staff Associate positions listed on these Check Lists with no deferment involved. This means that the selected candidate would come on active duty following internship and would immediately begin to fulfill his military obligation. Civilian appointments are also available.

After thorough review of all applications by the Institutes, a limited number of candidates will be selected for personal interviews to be held

during a 3-week period from May 8 through 26. Candidates should be prepared to come to NIH for an interview on short notice on any date within this period, at their own expense. All interviews are by invitation and are held only during this scheduled period.

The Clinical and Professional Services Section in the Clinical Center will set up the interviews and advise candidates when to report. Candidates are requested not to attempt to arrange their own interviews.

PART THREE

Program Areas for Which Candidates May Apply

EACH of the major NIH components has prepared a description of its program areas for which Associates may seek appointment. Due to diversity of the operations and programs within these major components, the descriptions do not follow a pattern. In effect, however, all of these descriptions are meant to anticipate the questions which applicants may have in selecting the program areas for which they wish to be considered. It should be noted that a candidate is not limited as to the number or kinds of positions for which he may apply.

National Cancer Institute

Director, Carl G. Baker, M.D.
Clinical Director, Alfred S. Ketcham, M.D.

Laboratories and Branches

Scientific Director for General Laboratories and Clinics, Nathaniel I. Berlin, M.D., Ph. D.
- Associate Scientific Director for Program Planning, Irvin C. Plough, M.D.
- Acting Chief, Laboratory of Biochemistry, Edward L. Kuff, M.D. Ph. D.
- Chief, Laboratory of Biology, Walter E. Heston, Ph. D.
- Chief, Laboratory of Biology, Walter E. Heston, Ph. D.
- Chief, Laboratory of Molecular Biology, Ira H. Pastan, M.D.
- Chief, Laboratory of Pathology, Louis B. Thomas, M.D.
- Acting Chief, Laboratory of Physiology, Nathaniel I. Berlin, M.D., Ph. D.
- Chief, Dermatology Branch, Marvin A. Lutzner, M.D.
- Chief, Endocrine Evaluation Branch, Erwin P. Vollmer, Ph. D.
- Chief, Immunology Branch, William D. Terry, M.D.

Chief, Metabolism Branch, Thomas A. Waldmann, M.D.
Chief, Radiation Branch, Ralph E. Johnson, M.D.
Chief, Surgery Branch, Alfred S. Ketcham, M.D.

Scientific Director for Etiology, Frank J. Rauscher, Jr., Ph. D.

Associate Scientific Director for Program, Gio B. Gori, Ph. D.

Associate Scientific Director for Viral Oncology, John B. Moloney, Ph. D.

Acting Chief, Viral Biology Branch, Robert A. Manaker, Ph. D.
Chief, Viral Carcinogenesis Branch, Robert J. Huebner, M.D.
Chief, Viral Leukemia and Lymphoma Branch, George J. Todaro, M.D.

Associate Scientific Director for Carcinogenesis, Umberto Saffiotti, M.D.

Chief, Biology Branch, Herbert J. Rapp, Sc. D.
Chief, Chemistry Branch, Harry V. Gelboin, Ph. D.
Acting Chief, Experimental Pathology Branch, Richard R. Bates, M.D.

Acting Associate Scientific Director for Demography, Marvin A. Schneiderman, Ph. D.

Chief, Biometry Branch, William A. Haenszel, M.A.
Chief, Epidemiology Branch, Robert W. Miller, M.D., Dr. P.H.

Scientific Director for Chemotherapy, C. Gordon Zubrod, M.D.

Acting Associate Scientific Director for Program, Seymour Perry, M.D.

Acting Associate Scientific Director for Clinical Trials, Paul P. Carbone, M.D.

Acting Chief, Medicine Branch, Vincent T. DeVita, M.D.
Acting Chief, Hematology and Supportive Care Branch, Edward S. Henderson, M.D.
Chief, NCI–VA Medical Oncology Branch, Oleg S. Selawry, M.D.

Acting Associate Scientific Director for Experimental Therapeutics, Vincent T. Oliverio, Ph. D.

Chief, Laboratory of Chemical Pharmacology, Vincent T. Oliverio, Ph. D.
Chief, Laboratory of Molecular Pharmacology, Kurt W. Kohn, M.D., Ph. D.
Chief, Laboratory of Toxicology, Robert L. Dixon, Ph. D.
Chief, Laboratory of Tumor Cell Biology, Robert C. Gallo, M.D.

Associate Scientific Director for Drug Research and Development, Saul A. Schepartz, Ph. D.

Associate Chief for Laboratory Research, Abraham Goldin, Ph. D.
Chief, Drug Development Branch, Harry B. Wood, Jr., Ph. D.
Chief, Drug Evaluation Branch, John M. Venditti, Ph. D.
Chief, Program Analysis Branch, Barbara R. Murray, M.A.

Acting Chief, Baltimore Cancer Research Center, Michael D. Walker, M.D.

Chief, Clinical Branch, Michael D. Walker, M.D.

Acting Chief, Laboratory of Pharmacology, Carl C. Levy, Ph. D.

Chief, Cancer Therapy Evaluation Branch, Stephen K. Carter, M.D.

General Laboratories and Clinics

A broad range of research is carried out in both basic laboratories and clinical branches under the general direction of Dr. Nathaniel I. Berlin.

In the Laboratory of Biochemistry, research is directed toward an understanding of neoplastic transformation in molecular terms. To this end, mechanisms of specific biochemical and ultrastructural differentiation are studied in a wide variety of cell systems. Granulocyte maturation, steroid induction of enzyme synthesis, the development and maintenance of immunoglobulin production, and the regression of certain tumors upon withdrawal of specific hormone support, are examples of processes currently under investigation with respect to both the biosynthetic events and the intracellular control mechanisms that might be involved. Other projects concern the occurrence and functional significance of cytoplasmic DNA in mammalian cells, the regulatory influence of cytoplasmic factors on nuclear DNA synthesis, the isolation and biochemical study of metaphase chromosomes, and the regulation of protein synthesis in cells infected with oncogenic viruses. Studies utilize normal tissues, various cultured cell lines, and a spectrum of transplantable tumors with useful biochemical attributes.

In the Laboratory of Biology, carcinogenesis is studied in the broad biological sense. Attention is given to the manner in which genetic, hormonal, immunological, and viral factors as well as chemical and physical carcinogens lead to the malignant transformation of the cell. Studies are aimed at revealing the nature of this transformation as it occurs under well controlled conditions in tissue culture. The mammary tumor virus and its variants in the mouse are studied as a model system in carcinogenic behavior of viruses. Genetic, immunologic, and chemical procedures are combined with electron microscopy. Studies of genetic control of blood and urinary proteins in mice and subhuman primates are also of primary interest.

Personnel of the Laboratory of Cell Biology have diverse interests focusing upon the study of transformation of a normal cell to a neoplastic cell. Techniques from the fields of virology, immunology, immunochemistry, biochemistry, biophysics, tissue culture, somatic-cell hybridization and electron microscopy are used. Some of the specific problems pursued are: genetic control of the synthesis of abnormal proteins produced by malignant cells (principally plasma cells), role of cell membranes in regulating differentiation and growth, identification and

study of tumor antigens and of the specific immune reactions initiated, solubilization and purification of transplantation and tumor antigens, influence of somatic cell hybridization on expression of genetically determined events, ultra structural study of viral oncogenesis.

The Laboratory of Molecular Biology investigates gene function in animal and bacterial cells. Studies are devoted to identifying factors which control and alter gene expression. Transcription is studied in purified cell-free systems, mutants defective in transcription are isolated and employed to detect these regulatory compounds. Other studies are directed towards investigating the molecular basis of genetic recombination. These studies employ the bacteriophage λ and its host, *E. coli.* Mutants defective in recombination are isolated and the nature of their defects analyzed by both genetic and biochemical methods.

The Laboratory of Pathology of the National Cancer Institute offers a 2-to-4-year training program for residents in pathologic anatomy in the Clinical Center, National Institutes of Health, Bethesda, Maryland. The program which is fully approved for Board certification provides well supervised instruction and experience in the performance of autopsies, surgical pathology and exfoliative cytology. Special training in the subspecialties of cardiac pathology, hematopathology and neuropathology can be arranged. Opportunity is provided for learning many research techniques, particularly electron microscopy, fluorescence microscopy, tissue culture, histochemistry, autoradiography and cytogenetics. Individual or collaborative participation in clinical or laboratory research projects by the residents and selected Research Fellows and Visiting Scientists is encouraged.

In addition to the autopsy, surgical pathology and cytodiagnostic services, the laboratory also carries on a broad research program in experimental pathology. Research projects include studies of oncogenic viruses and viral carcinogenesis, chemical carcinogenesis, immunopathology and tumor immunology, experimental embryology as related to cancer, and biochemical and ultrastructural studies of viruses and neopalstic cells.

In the Laboratory of Physiology there are a number of projects which bear on the physiological and biochemical properties of the growing tumor and its impact on the host. Approaches are made by studies on: control of protein synthesis in normal and tumor cells; the mechanisms of sythesis and secretion of hormones in the thyroid gland and thyroid tumors, and growth of the thyroid gland in response to stimuli; urinary excretion of purine and pyrimidine congeners and their relation to various types of leukemia; partition of the total energy expenditure of the tumor-bearing host between the host and the tumor; characterization and comparison of nucleic acids and nucleoproteins in bacterial and mammalian tissues; synthesis of nucleic acids with particular emphasis on elucidating the enzymatic control mechanisms in the intact

cell; protein synthesis in tissue culture during embryonic development. There are also a number of projects involving fundamental studies of the effects of radiation on proteins and on living organisms. These include studies of: effect of ionizing radiation on enzyme systems entailing the partial and complete destruction of active centers; antibody formation following multiple irradiation and immunization procedures; radiation damage and recovery of the hematopoietic system; and tissue transplantation and the immune response.

In the Dermatology Branch, studies are designed to identify and characterize the biologic behavior patterns of epithelial and lymphoid tissues in normal and pathologic circumstances, using primarily the techniques of biochemistry, electron microscopy, and tissue culture. The chemistry, structure, and function of keratin, melanins and epidermal cell organelles are being investigated, with particular reference to the genodermatoses of man and animals.

The Endocrine Evaluation Branch sponsors studies on endocrine factors in relation to breast cancer. This branch also plays an integral part in the Breast Cancer Task Force activities and its program for study and contol of breast cancer.

In the Immunology Branch, the mechanisms of normal and disordered immune response are under investigation. Physiochemical, immunochemical, tissue culture, isotope incorporation, and *in vivo* turnover techniques are used in research on the structure, biosynthesis, and genetic control of antibodies and of immune cell function. Cell antigens (histocompatibility, tumor specific and others), immune cell recognition systems and multiple aspects of cellular immunity are parts of fundamental and clinical studies in transplantation (bone marrow), tumor immunology, tumor immunotherapy, and immunodiagnosis of cancer.

The Metabolism Branch is studying the metabolism of tumors and the effects of tumors upon the metabolism of their hosts. To achieve these objectives, the research program includes studies of the anemia of cancer, porphyrin and bile pigment metabolism, nucleic acid metabolism, calcium metabolism, and serum protein metabolism in patients.

Investigations are also directed toward a broad range of imunological problems, especially as they involve immune deficiency states in man associated with a high incidence of malignancies. The studies are concerned with the mechanism of abnormalities of the circulating and cellular immune responses in patients with such disorders as agammaglobulinemia, the Wiskott-Aldrich syndrome, ataxia telangiectasia, and patients with protein-losing enteropathy and lymphocytopenia. Special attention is given to the study of the factors controlling immunoglobulin metabolism in man and in animal models of immunological deficiency states. In addition, studies are conducted on cell cooperation in the immune response on the role of the macrophage in the immune response, and on membrane associated antigen receptors of lymphoid cells.

The Radiation Branch is responsible for the development of new techniques in the treatment of cancer using irradiation alone and in combination with other modalities, especially chemotherapy. Clinical investigations receiving major emphasis are the malignant lymphomas and chronic leukemia, bone neoplasms, and cancer of the upper air passages and lungs. Active clinical studies are underway in the areas of tumor immunology and radiochemical modification of radiation response. Research in the Radiation Physics Section is closely integrated with clinical radiotherapy and includes computer applications to medicine. Laboratory research is designed to explore the feasibility of new therapeutic approaches and includes radiobiological studies with 14 MeV fast neutrons.

Of major interest to the Surgery Branch is control, through surgery, of pelvic malignancies, tumors of the head and neck area, skin, bone, and soft tissue tumors, and tumors of the urogenital system. Studies of patients with such malignancies are concentrated in three major areas: primary surgical therapy, various aspects of the host's immunological responses to cancer, and factors associated with the dissemination of cancer.

Etiology

In the Etiology area, a major responsibility of scientists under the direction of Dr. Frank J. Rauscher, Jr., is planning and implementing programmed research on cancer causation, patterns of cancer occurrence, and means for cancer prevention.

A program of virus-cancer studies is carried out in the Viral Biology, Viral Leukemia and Lymphoma, and Viral Carcinogenesis Branches under the Office of the Associate Scientific Director for Viral Oncology. Research activities with DNA and RNA viruses in biological systems range from the subcellular level to that of the intact host, including man. A special program is expanding basic and applied research on the possible viral etiology of leukemia. Institute scientists are collaborating with non-Federal investigators in multidisciplinary studies on animal tumor viruses and in the search for viruses in human cancer.

A special program to provide resource needs of cancer virologists, such as standardized cell lines and new varieties of research animals, is also located in the Viral Carcinogenesis Branch.

Chemical hazards in man's environment are of special concern to investigators in the Chemistry, Biology, and Experimental Pathology Branches under the Office of the Associate Scientific Director for Carcinogenesis. Emphasis here is placed on the interaction of host factors with multiple environmental factors.

The Epidemiology Branch plans and conducts studies using data from existing sources such as vital and employment records and clinical observations. These investigations seek clues to cancer causation through

analysis of interrelationships in the human and domestic animal populations with respect to their total environment and inheritance.

Some of the biostatistical studies carried out by the Biometry Branch are also concerned with the causes of cancer. Others are devoted to evaluating methods for diagnosing and treating cancer. In this connection, more than 100 hospitals in the United States are cooperating in a patient registration and followup program.

Chemotherapy

An intensive program of laboratory research and clinical investigation concerned with the chemical control of cancer is under the direction of Dr. C. Gordon Zubrod.

The Clinical Trials Area emphasizes a multifaceted approach leading to improved management and clinical control of patients with leukemia, lymphoma, and solid tumors with major interests in the acquisition of data from studies of cell kinetics, cytogenetics, biochemical growth characteristics of normal and malignant cells, immune mechanism, etc.

The Clinical Trials Area has as its objective the total care of patients with leukemia, lymphoma, and various solid tumors including lung, ovary, and breast cancer. Clinical Associates are assigned to the wards during their first year. The optimal use of new agents, combinations of drugs and maximal supportive care with platelet and leukocyte transfusion and patient protection techniques are investigated in a broad scale clinical program aimed at improving survival and eradicating the total tumor cell populations in these patients. During the second and third years, laboratory experience under the guidance of senior investigators is offered. Research interests include the clinical investigation of cellular kinetics, the pharmacology and physiologic disposition of new and established agents, the biochemistry of virus-host interactions, mechanisms of drug action and resistance, studies of immune mechanisms in cancer, bone marrow transplantation, immune suppressive effects of drugs, and the improvement in methods for separation, utilization and preservation of platelets and leukocytes. The Clinical Trials Area has three branches, Medicine, Hematology Supportive Care, and NCI–VA Medical Oncology. In addition, a center established to investigate Burkitt's tumor and other diseases in Uganda is supported and professional personnel is provided at Makerere University in Kampala, Uganda, Africa. Six Clinical Associates are chosen yearly. Appointments are for 2 years and extended to 3 years by mutual agreement. Credit for training in medical oncology to specialty board certification can be obtained. Selected individuals may be assigned to Kampala, Uganda, in Africa for their third or fourth years.

The Experimental Therapeutics Area studies many facets of the interactions between drugs and living materials. It includes biochemical

pharmacology, physiological disposition, drug metabolism, molecular pharmacology and comparative pharmacology. In addition, it works closely with the Medicine Branch on clinical research problems. In the Office of the Associate Scientific Director for Experimental Therapeutics, studies on the blood brain and blood cerebrospinal fluid barriers are conducted as well as investigations aimed at improving therapy of brain tumors and meningeal leukemia.

The Laboratory of Toxicology functions to investigate and describe the qualitative and quantitative toxicity of potential antineoplastic drugs using animal test systems. Attempts are made to define the predictability, reversibility, and mechanism of drug induced toxicity. Experimental treatment regimens are tested to attain the greatest therapeutic effect at the least cost in serious side effects. The functions of the laboratory are closely integrated with the development of new anticancer agents and ongoing clinical pharmacologic and toxicologic studies.

The Laboratory of Molecular Pharmacology is engaged in physical and biochemical studies on the effects of selected anticancer drugs on DNA. These drug effects are being studied in systems varying in complexity from purified DNA to the intact cell. The objectives are to understand how certain drugs interact with DNA and how the biochemical and physiological consequences of such interactions are expressed. The interactions of drugs with DNA are being examined by physical techniques, and the effects on DNA-primed RNA synthesis are being investigated in purified enzyme systems, isolated nuclei, and tissue-culture cells. In this regard, the need to understand the state of DNA and the control of its function in nuclei has recently led us to initiate studies on the relations between nucleic acids and proteins in structures such as chromatin. The approach has been to apply methods and data from molecular biology to problems in drug action, and also to use drugs to further our undesrtanding of cell physiology at the molecular level.

The Laboratory of Chemical Pharmacology is primarily engaged in studies related to the pharmacological disposition of antitumor agents and other drugs in man and animals through the use of established and newly developed analytical-biochemical techniques. Particular emphasis is placed on the study of the influence of simultaneously administered drugs on the distribution, protein binding, metabolism, excretion, and therapeutic activity of the individual agents; the pharmacokinetics of the entry of drugs across membranes into sensitive and resistant tumor cells; structure activity relationship of antitumor agents; new approaches to cancer chemotherapy in general, including studies with macromolecules and the nature of drug receptors; comparative pharmacology; the carcinogenic and other toxicological effects of drugs; enzyme systems involved in the metabolism of antitumor agents. Drugs of recent interest have been the folic acid antagonists, nitrosoureas, substituted hydrazines, plant alkaloids and DNA or RNA binding antibiotics. L-asparaginase

and poly I:C. In all areas of interest, both fundamental and mechanistic approaches are utilized.

The Laboratory of Tumor Cell Biology has several major research interests including studies on: (1) the controls of cellular growth, differentiation, maturation, and the process of malignant transformation in human cells are under intensive investigation; (2) mechanism of action of new antitumor agents and elucidating alterations involved in the development of resistance to drugs; (3) developments of biological or biochemical markers for the presence of small numbers of neoplastic cells; (4) cytogenetic techniques are an integral part of both cell kinetic and biochemical studies; (5) purification and biochemical and biological characterization of DNA polymerases from human cells and from oncogenic RNA viruses ("reverse transcriptase" or RNA-dependent DNA polymerase) have become a major aspect of the entire program. These studies are designed to aid in the understanding of the function of these enzymes, *e.g.*, appearance in the cell cycle, activity with certain compounds, role in cellular differentiation, and role in neoplastic transformation. The questions of whether any of the enzymes in cells are viral in origin and whether DNA polymerases of neoplastic cells differ qualitatively or quantitatively from those of normal cells are under intense study; (6) new antiviral agents are evaluated in a number of biological and biochemical systems; (7) the role of transfer RNA in differentiation and neoplastic transformation is also under investigaton.

The Baltimore Cancer Research Center conducts a collaborative program of clinical and laboratory research and training at the U.S. Public Health Service Hospital in Baltimore. The Clinical Branch is concerned predominantly with the evaluation of chemical agents for the control of neoplastic disease. Major clinical research programs include the use of chemotherapy (Dr. Peter Wiernik, Head) and radiation therapy (Dr. Kirkland Brace, Head), a neurosurgical brain tumor program concerned with diagnosis and therapy of primary and secondary cancer of the central nervous system (Dr. Michael Walker, Head), and major microbiology programs in infectious complications occurring in the treatment of malignant disease (Dr. V. Young, Head), including the evaluation and use of protected patient environment employing the concept of laminar air flow. A blood component replacement therapy program including leukocytes and platelets and clinical pharmacologic investigation of anticancer drugs is also in progress as are computer and other research programs in patient care. The primary clinical material is that of leukemias, lymphomas, central nervous system malignancies, and selected other cancers. The clinical program is at the PHS Hospital where there are fully approved residency programs in the major medical specialties.

The Laboratory of Pharmacology is concerned with basic research programs in biochemical pharmacology of chemotherapeutic

agents (Dr. N. Bachur, Head) and drug enzyme interactions (Dr. C. Levy, Head). An active clinical and laboratory investigative program of tumor immunology (Dr. M. Mardiney, Head) completes the program.

Drug Research and Development is engaged in a multidisciplinary approach to the fundamental and developmental aspects of cancer chemotherapy. Through contracts and direct laboratory operations it carries out programs directed toward the development of new and better antitumor agents: The Drug Development Branch is charged with responsibility for the development of new agents from synthetic and natural sources and for production and formulation of drugs for pharmacologic and clinical studies; the Drug Evaluation Branch is concerned with the evaluation of such agents in experimental test systems predictive for clinical utility, recommendation of new agents as candidates for clinical trial, detailed studies of optimal drug dosages and regimens, mechanisms of drug action, means of overcoming the development of resistance to treatment, and the development of improved drug screening systems; in the Office of the Chief, research programs are concerned with fundamental chemotherapeutic, biological, biochemical and immunological investigations of the mechanism of action of antitumor and antiviral agents, new therapeutic models, metastasis, drug resistance, animal genetics and disease control; studies are correlated with the clinic in the development of modalities of therapy, special problems and therapeutic principles.

The Cancer Therapy Evaluation Branch is responsible for coordinating and monitoring the clinical trials performed with the new anti-cancer agents sponsored by the Chemotherapy Program. This involves liaison with the Intramural Clinical Program, the Extramural Chemotherapy Cooperative Group Program and the expanding area of clinical contracts. In addition, the branch is responsible for international clinical liaison and world-wide clinical trial surveillance.

The Drug Liaison and Distribution Section (Dr. John S. Penta, Head) handles the liaison with the Food and Drug Administration as well as coordinating the details of drug distribution and protocol handling.

The Clinical Trial Surveillance Section (William T. Soper, Head) is responsible for the handling of the massive clinical data input into the branch in such a way as to make it readily accessible for evaluation and integration.

Internally, the branch handles the inflow of both preclinical and clinical information into the various decision networks of the Chemotherapy Program linear array system.

National Eye Institute

Carl Kupfer, M.D., Director

The National Eye Institute conducts, fosters and supports research and training on the cause, natural history, prevention, diagnosis, and treatment of disorders of the eye and visual system.

The Institute selects three Clinical Associates from those candidates who have completed an accredited 3-year ophthalmology program. Clinical Associates spend time in both clinical and laboratory research, including patient care activities.

Research Associates selected by the National Eye Institute usually do not participate in the CORD Program and therefore are called to duty one year after graduation.

In selection of Clinical and Research Associates, preference will be given to those who will continue their research training either at the National Institutes of Health or in an academic setting elsewhere with an eventual career in full-time academic ophthalmology.

Laboratory and Clinical Research

The National Eye Institute has developed its clinical and research program into two major branches, the Laboratory of Vision Research and the Clinical Branch. The Laboratory of Vision Research plans and conducts fundamental laboratory research on the visual system. This includes anatomy, biochemistry, physiology, embryology, pharmacology, and experimental pathology of the visual system.

The Clinical Branch plans and conducts clinical research into the causes, prevention, diagnosis, and treatment of diseases of the visual system. It translates laboratory research results into clinical application and directs and administers the Institute's clinical care program and assures proper functioning of the eye ward and clinic in the NIH Clinical Center.

It is the Clinical Branch's responsibility to investigate the causes and prevention of blindness. The major areas under study are glaucoma, retinal degenerative diseases, especially inherited dystrophies, corneal disease, and inflammatory diseases.

(1) In glaucoma, studies are directed to the understanding of intraocular fluid dynamics in the normal and glaucomatous eye. As a consequence of these studies relating to the regulation of eye pressure, selective new drugs and surgical procedures which are capable of normalizing the intraoccular fluid dynamics and thereby lowering the pressure within the eye are constantly sought and tried clinically.

(2) In the retinal degenerative disorders, there is a premature death of certain cells within the retina which is the neural and biochemical

mediator of vision. These disorders are mostly inherited and at the present time, poorly understood. Much of the research effort in the past has been confined to areas of diagnosis, classification, and family studies. It is hoped that future research will be directed to the anatomical, biochemical and physiological basis of these disorders.

(3) Corneal diseases which are unresponsive to conventional forms of therapy will be treated by new medical and surgical techniques.

(4) The inflammatory diseases under study include sympathetic ophthalmia and Behcet's disease. Both new diagnostic and therapeutic techniques are under investigation.

The Laboratory of Vision Research is composed of the following disciplines:

(1) *Experimental Embryology.* The goals are to identify and analyze the myriad tissue interaction that control the orderly growth of the vertebrate eye and assure that each ocular part develops a size, shape and orientation appropriate to its function in this sense organ. More specifically, the researchers are determining which tissues are responsive to such influences, the duration of these potencies and competencies during embryogenesis, the species and tissue specificities of these interactions, and the nature of these tissue interactions which control ocular morphogenesis.

(2) *Pharmacology.* This laboratory is presently conducting studies on the physiology and pharmacology of intraocular pressure. The ultimate goal is to ascertain how glaucoma is produced and to find drugs which can effectively control this disease. Studies are also underway to determine how the intraocular blood vessels respond to drugs. The object of this latter study is to make available to the clinician, drugs which have specific types of activity on blood vessels.

(3) *Biochemistry.* Investigations are underway on the chemical structure of the visual pigments, their attachment to the disc membrane of the outer segment and the role of rhodopsin in the visual cycle. In addition, the fine structure and pathological anatomy of the retina in experimental animal models is being investigated by transmission and scanning electron microscopy, light and electron auto-radiography and histochemistry. Finally, metabolic pathways of lens and cornea are being investigated for insights into biochemical and physiological derangements in cataracts and corneal disease.

(4) *Ophthalmic Physiology.* This section is studying the responses of single nerve cells in the visual nervous system of the rhesus monkey. The purpose of this work is to understand how each nerve cell functions in contributing to visual sensations such as color, shape, movement, depth, etc.

The technique employs fine glass micro-electrodes which can be inserted into the brain in order to record from single nerve cells. It uses refined optical methods to enable an experimenter to observe the retina

while stimulating it with punctate spots or lines of colored light whose movement and shape can be quantitatively controlled. It requires electrophoresing particles of dye into single cells whose responses have been studied and then finding these particles precisely within the brain after the animal is sacrificed.

In the next few years the investigator expects more time will be devoted to linking anatomy with physiology, that is to determine what types of cells (anatomically) perform what sorts of functions (physiologically).

National Heart and Lung Institute

Donald S. Fredrickson, M.D., Director of Intramural Research

Frederic C. Bartter, M.D., Clinical Director

A. Associate Program in Medicine and Basic Science

The National Heart and Lung Institute currently appoints three Research Associates and six Clinical Associates for a 2-year period beginning each July 1. Several Staff Associates are also usually appointed in one or more of the Intitute's laboratories. For those who are interested in lengthening their period of research experience, these appointments may, by mutual agreement, usually be extended for a third year.

Candidates may apply for one or more types of Associate positions. In selection of Associates preference is given to candidates who intend to devote a significant portion of their career to research. Because of the diversity of the Heart and Lung Institute program, special interest in cardiovascular disease is not an essential requirement.

Research and Clinical Associates

Candidates for Research and Clinical Associate positions have only one interview in the Heart and Lung Institute. Each Associate who is chosen is free to select his own area of research assignment. After his appointment and prior to his entering on duty, he will make a separate visit, at Institute expense, to select the laboratory in which he will work. The choice is based on the background and interests of the Associate and appointment to the chosen laboratory is contingent only on the ability of that particular laboratory to furnish proper supervision and facilities. (On the basis of past experience, it appears virtually certain that each Associate will be able to work with the group of his choice.) The level of research responsibility and freedom will depend upon his training and experience as well as his desires.

Each Associate will devote his time primarily to research in the laboratory under the immediate supervision of a preceptor in an area of his selection. Each is expected to engage in appropriate course work in the basic, medical, and allied sciences as well as tutorial seminars, and to take an active part in the journal club and other exercises of his laboratory.

Research Associates. These appointments are designed to give physicians an opportunity to improve their background for a career in basic medical research. Usually physicians enter the appointment after completing internship and 1 year residency, but there are no specific require-

ments for postgraduate training after the M.D. degree. No clinical assignments are involved (unless the Associate has chosen a laboratory involved directly in clinical investigation), but the Associates are welcome to attend any of the clinical teaching exercises.

Clinical Associates. These appointments are designed to give physicians training in both clinical and basic research. Candidates must have completed a minimum of 1 year of internship plus 1 year of residency in internal medicine by the starting date of their appointment.

Clinical Associates will be responsible, under the guidance of investigators on the Heart and Lung Institute staff, for the medical care of patients during 10 of the first 14 months of their service. During this time they will rotate through the four medical services that serve the clinically oriented Branches of the Heart and Lung Institute. These services occupy 85 beds and include: (1) Cardiology; (2) Endocrinology; (3) Experimenal Therapeutics; and (4) Molecular Disease.

The clinical period is one of intensive training under direction of the Clinical Director and staff. It offers exposure to case material of an extraordinary range and to highly sophisticated approaches to investigation of disease.

The Clinical Associate devotes both his time off the wards and a full 14 months of his 2-year assignment to laboratory research under direction of a preceptor *in any one of the Heart and Lung Institute laboratories, either clinical or nonclinical.* No clinical responsibilities are required during the optional third year.

Staff Associates. Laboratories within the Heart and Lung Institute sometimes have openings for Staff Associates appointed from the Matching Program. When such appointments are available they are listed in the Program Area Selection Check List for the Institute. Selections for those positions are made by the Chief of the Laboratory. The position of Staff Associate is otherwise comparable to that of Research Associate.

Formal Instruction

The major form of didactic postgraduate instruction is through the evening courses offered by The Graduate Program of the Foundation for Advanced Education in the Sciences, Inc., and through the NIH tutorials. Research, Clinical, and Staff Associates are expected to take advantage of this academic work.

B. Associate Program in Surgery

The Surgery Branch of the National Heart and Lung Institute appoints approximately five Associates in Surgery for a 2-year period beginning each July 1. The program is primarily designed for young surgeons with primary interests in cardiovascular surgery and cardiovas-

cular physiology. In making appointments, preference will be given to candidates contemplating a career in a research or academic atmosphere. Candidates must have completed an internship and at least 1 year of surgical residence by the starting date of their appointment.

Laboratories and Sections

The laboratories and sections of the National Heart and Lung Institute, all of which are open to Clinical and Research Associates for their research work, are listed below with the names of their chiefs and a brief summary statement indicating the breadth of activities. Candidates desiring further information may obtain a current bibliography summarizing the activities of the current staff by writing to Dr. Donald S. Fredrickson, Director of Intramural Research, National Heart and Lung Institute, Bethesda, Md. 20014.

Laboratory of Biochemical Genetics (Chief, Dr. Marshall Nirenberg). Biochemical aspects of cell differentiation are studied, particularly regulated steps required for the development of clonal lines of mammalian neuroblasts *in vitro*.

Laboratory of Biochemistry (Chief, Dr. Earl R. Stadtman).

Section of Enzymes (Head, Dr. Earl R. Stadtman). Studies of diverse enzyme systems that offer unique opportunities to elucidate a number of basic biochemical phenomena, namely, those concerned with vitamin-coenzyme function, the cellular regulation of metabolism, the energy-dependent transport of metabolites across membrane barriers, and mechanisms of enzyme action.

Section on Cellular Physiology (Head, Dr. Wayne Kielley). This section conducts studies of the structural basis for the biochemical properties of protein molecules and their integrated function in cellular structures. Primary emphasis is on muscle contraction and other motile systems.

Section on Cellular Biochemistry and Ultrastructure (Head, Dr. Edward D. Korn). This section studies structural-functional relationships at molecular and cellular levels. Present activities are focused on the biochemistry of the plasma membrane in relation to endocytosis and the molecular and ultrastructural basis of cell motility.

Laboratory of Chemical Pharmacology (Acting Chief, Dr. James R. Gillette).

Section of Clinical Pharmacology. This section explores mechanisms of idiosyncratic effects of drugs. Also explores biochemical and physiological mechanisms of drug action, including

the functions of the autonomic nervous system, the role of adrenocortical, thyroid and other hormone systems in regulating the autonomic and central nervous systems and the processes that control the tissue levels of biogenic amines, acetylcholine, and c–AMP.

Section of Drug-Tissue Interaction (Head, Dr. Watson D. Reid). Studies the mechanism by which drugs, or their chemically active metabolites, produce pathological lesions in liver, kidney, bone marrow and brain by reacting covalently with tissue macromolecules.

Section on Enzyme Drug Interaction (Head, Dr. James R. Gillette). Studies various aspects of drug disposition including the mechanism of drug-metabolizing enzymes in liver microsomes, the factors which alter the activity of these enzymes, and the relationship between the metabolism and toxicity of drugs.

Section on Organic Chemistry (Head, Dr. Elwood O. Titus). Studies isolation and characterization of those cellular components, usually membrane proteins, which serve as the targets for drugs and hormones affecting the cardiovascular system and carries out physical chemical studies of the mechanisms by which drugs interact with these components.

Section on Physiology (Head, Dr. Harriet M. Maling). Studies the cardiovascular, behavioral, and other physiological responses to drugs and correlates these responses with biochemical effects. Studies the role of endogenous histamine and the influence of the sympathetic and parasympathetic nervous system, the pituitary gland, the adrenocortical system, and other endocrine glands on local inflammation and hepatotoxicity induced by drugs and chemicals. Explores the role of binding of compounds to liver phospholipids as a possible mechanism of hepatotoxicity.

Laboratory of Chemistry (Chief, Dr. Henry M. Fales). Conducts research into methods for the strutcural analysis of organic compounds specifically *via* mass spectrometry, X-ray crystallography, nuclear magnetic resonance, etc., in addition to classical methods of chemical degradation. Also studies biosynthetic pathways *via* tracer techniques and chemical synthesis.

Laboratory of Kidney and Electrolyte Metabolism (Chief, Dr. Jack Orloff).

Section on Electrolyte Transport

Section on Experimental Cardiovascular Diseases

Section on Renal Mechanisms

Section on Membrane Metabolism

This Laboratory conducts research on the mechanism and regulation (hormonal and otherwise) of a variety of transport processes in systems including the intact kidney, isolated segments of renal tubules, toad bladder, erythrocyte, and muscle.

Laboratory of Technical Development (Chief, Dr. Robert L. Bowman).

Conducts research into instrumentation and methodology applicable in heart and biomedical research. The scope of the program extends from highly specialized research ultramicro methods to practical clinical instrumentation.

Section on Pulmonary and Cardiac Assist Devices (Head, Dr. Theodor Kolobow). Conducts a program to develop and clinically apply devices for extracorporeal support of the respiratory and circulatory systems. This program includes the development of improved blood oxygenators, blood pumps, and control systems.

Cardiology Branch (Chief, Dr. Stephen E. Epstein).

Section on Cardiovascular Diagnosis (Head, Dr. David L. Glancy). Investigations are oriented toward the diagnosis of acquired and congenital heart disease, the evaluation of operative and nonoperative forms of treatment, and the elucidation of mechanisms responsible for the hemodynamic changes produced by heart failure.

Section on Cardiovascular Pharmacology (Head, Dr. Theodore Cooper). Current work is concerned with a comprehensive study of the terminal nervous innervation of the heart and how it is altered following denervation. Cellular effects of drugs are also under investigation in isolated cardiac tissue. The action of inotropic agents under conditions of limited myocardial oxygen supply is under investigation.

Section on Clinical Physiology (Head, Dr. Stephen E. Epstein). Research objectives are aimed toward an understanding of the physiologic and biochemical mechanisms responsible for control of the normal heart and circulation, an elucidation of the alterations produced by ischemic and non-ischemic heart disease, and an evaluation of interventions designed to reverse the biochemical and, thereby, the physiologic aberrations of function.

Endocrinology Branch (Chief, Dr. Frederic C. Bartter).

Section on Steroid Metabolism and Hypertension.

Section on Mineral Metabolism. The principal research of this Laboratory is involved with the functions of the adrenal glands, the parathyroid glands and bone metabolism, the pituitary gland,

and the kidneys. Basic laboratory work (concerned with underlying biochemical, physiochemical or physiological mechanisms) and clinical research are directed towards (1) steroid metabolism and the pathologic physiology of hypertension, (2) metabolic bone disease and the pathogenesis of nephrolithiasis, and (3) a wide variety of endocrine disorders.

Experimental Therapeutics Branch (Acting Chief, Dr. Harry R. Keiser). Offers a spectrum of research opportunity ranging from basic biochemistry and pharmacology to the study of chemical factors in disease and clinical response to drugs. Current studies encompass disorders of amine metabolism (catecholamines, serotonin), biochemistry of sleep and collagen disease. Studies on essential hypertension are conducted both in man and in experimental models in the rat.

Section on Biochemical Pharmacology (Head, Dr. Walter M. Lovenberg). Conducts a broad research program in the biochemistry and pharmacology of neurohumoral substances. Studies relate to the properties of their synthetic and degradative enzymes. Other areas of current research are the chemical and physical properties of certain metalloproteins, specifically, ferredoxin and rubredoxin.

Section on Neuroendocrinology (Head, Dr. Robert I. Henkin). Devoted to the study of the interrelationships between the nervous and the endocrine systems in three interrelated areas: (1) the effects of steroid hormones on nervous system activity as well as steroid localization and metabolism in the nervous system; (2) mechanisms of function of gustation, olfaction and audition as represented in various disease states; and (3) the effects of trace metals in neuroendocrine metabolism, in various altered metabolic states and as indicators and treatment in various gustatory and olfactory abnormalities.

Section on Physiological Chemistry (Head, Dr. John J. Pisano). Studies concerned with the identification, biosynthesis, assay, and metabolic significance of biologically active peptides, related precursors and enzymes. The scope of activities includes the development of necessary new analytical procedures and the study of normal and pathological conditions in man at the molecular level.

Molecular Disease Branch (Chief, Dr. Donald S. Fredrickson).

Section on Genetics and Lipid Biochemistry (Head, Dr. Howard R. Sloan).

Section on Lipoproteins (Head, Dr. Robert I. Levy).

Section of Molecular Diseases (Head, Dr. Donald S. Fredrickson).

Section of Molecular Structure.

Section on Peptide Chemistry (Head, Dr. Bryan Brewer).

The work of these five sections is primarily concerned with an integrated study of fat transport in plasma. This includes the structure, metabolism, and functions of lipoproteins, the structure of apolipoproteins and other peptides and polypeptides, and genetically determined disorders relating to lipid transport and metabolism and to atherosclerosis. The research carried out by Associates is often in collaboration with members of more than one of these sections.

Section on Metabolism (Head, Dr. Martha Vaughan). Major areas of research interest are: (1) the mechanisms underlying hormonal control of lipolysis in fat cells, with emphasis at present on characterization of the hormone sensitive lipase and elucidation of the manner in which insulin, prostaglandins, and adrenal steroids affect the formation, degradation, and action of cyclic AMP; and (2) the role of cyclic AMP, cyclic GMP, and compounds that influence the metabolism of these nucleotides (e.g., prostaglandins, adrenal steroids) in regulation of growth and morphology of mammalian cells grown in culture.

Section on Molecular Hematology (Head, Dr. W. French Anderson). Concerned with investigations into the mechanism and regulation of mammalian protein synthesis, specifically relating to hemoglobin and diseases involving the regulation of hemoglobin synthesis.

Pulmonary Branch

The Lung Laboratory is in the process of formation. It will include a broad approach to both pulmonary physiology and the organ functions of the lung, including clinical investigation. A pulmonary function laboratory has been established. In formation are units devoted to protein synthesis within the lung and morphology. This Branch will undergo major expansion within the next several years.

Section on Experimental Atherosclerosis (Head, Dr. Donald L. Fry). The Section program is directed toward experimental evaluation of the pathological, physiological, biophysical, chemical and histologic processes involved in the genesis of atherosclerosis. These studies are carried out using tissues from both animal colonies and human subjects.

Section of Pathology (Head, Dr. William C. Roberts). This Section is concerned with the study of morphologic aspects of cardiovascular disease and correlating them with functional derangements. Morphologic analyses include electron microscopy.

Surgery Branch (Chief, Dr. Andrew G. Morrow).

National Institute of Allergy and Infectious Diseases

John R. Seal, M.D., F.A.C.P., Scientific Director

John E. Tobie, Ph. D., Assistant Scientific Director for Laboratory and Clinical Research

The NIAID annually appoints Associates for the Laboratories described below. Clinical Associates are selected by the Clinical Director, are appointed to the Laboratory of Clinical Investigation, and begin after one year of residency training. Research Associate appointments in the other laboratories may begin after internship or residency training. In general, those appointments which begin after one or more years of residency training have some degree of responsibility for human subjects in the research program but are not otherwise different from those which begin after internship. About one-half of the total Research Associates have been given CORD deferments in past years.

Appointees through the Early Commissioning Program will be regarded as appointees through other programs and final identification as to positions for which they are being considered and as to whether or not the position will afford one or more years of residency training before entry will be made to prospective candidates at the time of interview.

Specific answers may be obtained for any questions or additional information obtained by applicants from Dr. John R. Seal, Scientific Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md. 20014. This can include rosters of scientific staff, summaries of research, or information about possible opportunities not listed under the laboratories. In writing, please be as specific as possible as to interests of applicant and information desired.

The Laboratory of Clinical Investigation (Sheldon M. Wolff, M.D., F.A.C.P., Clinical Director)

The National Institute of Allergy and Infectious Diseases appoints six to eight Clinical Associates. Appointments are made for 3 years. Ward medical care duties occur during the first year, and no assigned clinical responsibilities are made during the second or third year except as dictated by the needs of the Clinical Associates' research.

There are 52 research beds. Clinical Associates consult on clinical infectious disease problems in other Institutes and at the National Naval Medical Center. Each Clinical Associate selects his own area of investigative interest under the general preceptorship of the Clinical Director and the senior members of the staff of the Laboratory of Clinical Inves-

tigation. Emphasis is placed on the conduct of laboratory and clinical research designed to provide the basic training necessary for a career in clinical investigation.

Opportunities exist for research in a wide variety of areas of infectious and immunological disease. Examples of studies now in progress are:

- Elucidation and evaluation of immunologic and nonimmunologic events induced in humans and animals by viral infection or vaccination.
- Antifungal chemotherapy, analysis of antigenic constituents of fungi, and development of diagnostic skin and serologic tests for mycoses.
- Pathogenesis of both experimental and clinical fevers.
- The role of the granulocyte in resistance and response to infection.
- The mechanism of immune damage and the role of complement in immunological reactions.
- Biochemical and morphologic properties of lysosomes and the lysosomal enzymes of human leukocytes to determine their role in the pathogenesis of certain inflammatory diseases.
- The biochemical response in lymphoid cells following antigenic stimulation in normal and immunologically impaired subjects.
- The pathogenic mechanisms of the aspirin sensitivity-asthma syndromes.
- The structure and function of immunoglobulins of human and lower animal origin.
- The application of electron microscopy, autoradiographic, and cytochemical techniques to studies of cellular interactions in immunologic information processing both in humoral and cellular events.
- The role of kinins in the pathogenesis of reactions of the immediate hypersensitivity type.
- Research in both the clinical and laboratory aspects of parasitic diseases.

Further information can be obtained if inquiries with specific questions are addressed to Dr. Sheldon M. Wolff.

The Laboratory of Viral Diseases (Wallace P. Rowe, M.D., Chief) conducts research on the basic biology and ecology of chronic and persistent virus infections, with particular emphasis on oncogenic viruses, and on host antiviral defense mechanisms.

Studies of tumor viruses are concentrated on murine leukemia viruses, SV40, adenovirus-SV40 hybrid viruses, and Marek's disease of chickens. These studies include investigations of the interactions between defective and competent viruses, etiology of naturally occurring animal tumors, serologic characterization of viral products, and genetics of the viruses.

The mechanism of action of interferon and inducers of interferon is studied by biological and biochemical approaches. The laboratory will

be participating in clinical evaluation of interferon inducers in a variety of diseases.

The Laboratory of Biology of Viruses (Norman P. Salzman, Ph. D., Chief) is primarily concerned with the molecular events involved in virus replication. Investigations are also conducted to define the basis for the pathogenic effects of viruses on cellular functions. Biosynthesis of the nucleic acid, protein and carbohydrate components of virus particles and factors governing their assembly are under study as is the mode of action of certain specific antiviral substances. These studies are carried out with both lytic and oncogenic viruses. Fundamental biochemical and biophysical studies are also carried out with uninfected cells. The mechanisms by which normal cells are transformed to an oncogenic state are also studied.

Parallel studies to those on viral synthesis seek to define the physical and chemical makeup of the purified virus itself, utilizing electron microscopy, ultracentrifugation, and nucleic acid and protein analysis.

Other programs investigate the isolation and characterization of mutated viruses. Studies are conducted on the relationship between mutations in the viral genome and biochemical alterations in the infectious cycle.

The staff includes persons trained in biochemistry, medicine, microbiology, physical chemistry, and organic chemistry. The program for associates is designed to provide them with a full understanding of modern trends in molecular biology and to enable them to apply biochemical and biophysical methods in dealing with fundamental problems in virology, cell biology and medicine.

The Laboratory of Infectious Diseases (Robert M. Chanock, M.D., Chief) is concerned with the basic behavior of viral and mycoplasmal pathogens which play an important role in acute infectious diseases of man. The importance, disease manifestations and ecologic properties of various respiratory tract pathogens are defined during the study of individuals with naturally acquired disease. Supplementary information is obtained from detailed investigation of experimentally infected volunteers in an attempt to define the pathogenesis of disease and the factors involved in the hosts' resistance to both infection and illness. The techniques of microbial genetics are employed to study the nature of virulence and to select attenuated mutants which are then evaluated for their usefulness in vaccination against natural disease.

Biophysical techniques are used to define the subparticulate structure of viruses and to search for certain fastidious agents, such as coronaviruses and hepatitis viruses, which cannot be detected in standard tissue culture systems. Appointees can expect to receive training in basic biophysical and biological characterizations of viruses and mycoplasmas, microbial genetics, immunologic methods used in the study of respiratory tract

disease and epidemiologic techniques employed in defining the ecology of agents which cause acute infectious diseases. Some appointments are made for 3 years.

The Laboratory of Immunology (William E. Paul, M.D., Chief) is engaged in the study of various aspects of cellular immunology, immunogenetics and immunochemistry, particularly as they bear on a fuller understanding of the biological significance of the immune response and on the role of immune mechanisms in both the prevention and pathogenesis of human disease.

Arease of active investigation now include the study of the antigen-binding receptors of immunocompetent cells and the mechanisms of specific interaction between such cells; the detailed examination of specific immune responses which are under genetic control and the study of the mechanisms by which such genetic control is exerted; the nature of allotypic determinants of rabbit and mouse immunoglobulins and the use of such determinants to study the genetic control of immunoglobulin synthesis; the study of the role of complement in various immunobiologic and immunopathologic phenomena, through the use of a group of guinea pigs with a total lack of the fourth component of complement; the role of cellular immune responses in tumor immunity and the development of models to study immunotherapy of tumors.

Further, an active inquiry into the high degree of specialization of various immunocompetent cells is underway and studies of immunogenicity through the use of both highly purified peptide antigens and hapten-carrier conjugates are being pursued.

Associates will have the opportunity to participate in studies in one (or more) of these areas under the preceptorship of one of the senior members of the laboratory. In the course of their work, appointees should receive a thorough grounding both in conceptual and technical aspects of immunology.

The Laboratory of Microbial Immunity (John E. Tobie, Ph. D., Chief; Richard M. Asofsky, M.D., Assistant Chief) is primarily concerned with the elucidation of basic mechanisms involved in both the cellular and humoral immune responses to microbial and tissue antigens. In addition to its conventional facilities the Laboratory maintains a special facility for germ-free animals, for use in studies in which it is desirable to minimize exposure to naturally occurring antigens or in which low rates of immunoglobulin synthesis before experimental manipulation are necessary.

Several different major areas of investigation, each employing a wide variety of basic immunological techniques, offer the Associate the opportunity to receive comprehensive exposure to both the technical and theoretical aspects of immunology. The mechanisms involved in the induction and control of immunoglobulin synthesis are currently being examined

in detail. The significance of interaction among different kinds of lymphoid cells in the induction and manifestation of immunity is being examined in two systems: the graft-*versus*-host reaction as a model of homograft immunity, and the antibody response to pneumococcal polysaccharides as a model of humoral immunity. The distribution, ontogeny, and susceptibility of the interacting components to various treatments are each being examined as are methods of fractionating lymphoid cells into functionally purified subpopulations. Auto-immune phenomena are studied using allergic thyroiditis and retinitis as models: factors regulating the development and severity of disease such as the interaction of sensitized cells and antibody in the production of immune tissue injury, and specific methods of preventing or ameliorating such disease are being investigated. Finally, the nature of the immune response to protozoal parasites, and the antigenic and genetic requirements for expression of this immunity are being extensively studied.

The Laboratory of Parasitic Diseases (Franklin A. Neva, M.D., Chief) is engaged in fundamental and applied studies of parasitic diseases of man. These studies are conducted at three geographical locations.

At Bethesda, the largest facility, research is centered principally on basic studies of toxoplasmosis, trypanosomiasis, leishmaniasis, schistosomiasis, amebiasis, and filariasis by various approaches. One is to apply the basic sciences, such as biochemistry or immunology, to the study of different parasites. For example, one group with broad interests in comparative physiology of parasites is investigating biochemical mechanisms of energy transfer in vertebrate and invertebrate cells. Specialized optical techniques, including interferometry, are used for qualitative and quantitative studies of host-parasite interactions at the cellular level. Other workers are studying the neuro-biology and the growth and differentiation of nematodes. Ultrastructure of parasites and relationship of their structures to function represents still another area of study. A second research approach is the study of a specific parasitic disease entity in laboratory models and in man. Examples of current work are investigations of schistosomiasis, filariasis, and Chagas' disease, with particular emphasis upon pathogenesis of disease and immunity and hypersensitivity as factors in the host-parasite relationship. Human studies involve both patients at the NIH and to a limited degree people in various tropical countries.

The research program on malaria covers many different aspects of the subject and includes work on chemotherapeutic agents, biology of human and simian malarial parasites, the arthropod vectors of malaria and the immunology and pathophysiology of malaria. Much of this work is done at Bethesda, but there are also off-site laboratories at Chamblee, Georgia, which are uniquely equipped for work with malaria in primates, includ-

ing an insectary for work with malaria vectors. Closely related to the unit in Chamblee is a facility in adjoining Atlanta for work with malaria in human volunteers. The combined facilities offer almost unparalleled opportunities for work on malaria in man or in animal models and on all stages of the life cycle of the parasite.

A third component of the Laboratory (under the direction of Dr. Leon Rosen) is located in Honolulu, Hawaii, where research focuses upon parasitic as well as viral diseases of particular importance to the Pacific area. The isolated ecologic environment of some of the Pacific Islands offers certain unique research opportunities. Specific areas of study include eosinophilic meningitis, arboviruses, transmission of toxoplasmosis and competition between mosquito species in nature.

The Laboratory of Microbiology (Roger M. Cole, Ph. D., M.D., Chief) is engaged in basic studies of bacteria, mycoplasma, and fungi. Streptococci, staphylococci, bacilli, and a few gram-negative bacteria are the principal bacterial subjects of current investigation. Areas of study include streptoccocal genetics and bacteriophage; the nature, identification, induction, and reversion of bacterial L-phase growth and its role in pathogenicity and disease; the role of iron in nonspecific immunity and in bacterial metabolism; bacterial cell walls and autolytic enzymes; isolation and function of membranous organelles from cocci; the electron transport system of hydrogen-utilizing autotrophs; composition, synthesis, and modification of naturally-occurring and synthetic antimicrobial agents; the nature and isolation of some *Mycoplasma* antigens; ultrastructure of bacteria, bacterial mutants, and other microorganisms; pathogenesis of lesions induced by streptococcal fractions and products; and the fate of phagocytosed bacteria.

There are also a variety of investigations on the taxonomic relationships among mycoplasma and on the pathogenicity of these organisms in animal and human diseases. Medical mycology research includes studies on physiology, nutrition, experimental chemotherapy, genetics, immunology and immunochemistry.

The Immunology Section is concerned with the genetics and mechanisms of hypersensitivity reactions, the relationship of microbial antigens to tissue antigens, and the role of bacterial components in adjuvants.

The Middle America Research Unit (Karl M. Johnson, M.D., Director) is located in the Panama Canal Zone and is a joint enterprise of the PHS and the U.S. Army. This well-equipped laboratory is engaged in the study of Bolivian hemorrhagic fever, a viral disease with high morality. Areas emphasized include epidemiology and field ecology in Bolivia, comparative virological investigation of the causative agent and its immunologic relatives, and the biological behavior of the virus in its natural rodent reservoir *Calomys callosus*. Epidemiological work on several arthropod-transmitted virus diseases such as Venezuelan equine

encephalitis and St. Louis encephalitis continues. Field studies in several countries provide materials for laboratory-based efforts to develop new techniques for understanding the complex life-cycles of these infections in the tropics. Recent work documented the importance of geographic variation in virus strains; immunological studies are in progress to assess the importance of this finding both in terms of evolutional biological theory and practical public health application. The ecology of vesicular stomatitis virus infection is being investigated. Since the mode of virus transmission is unknown, work includes field observations, experimental studies of concern arthropods, and virological and immunological investigations of virus behavior in tropical vertebrates.

Through liaison with the U.S. Army component, opportunities are available for laboratory and field study of certain parasitic diseases, particularly toxoplasmosis, leishmaniasis, and American trypanosomiasis.

The Rocky Mountain Laboratory (Herbert G. Stoenner, D.V.M., Director), located at Hamilton, Mont., is internationally recognized for research on rickettsial and tick-borne diseases. In medical entomology and acarology, principal projects include biology and systematics of ticks and mites, ecology of selected tick- and mosquito-borne viruses, and general and subcellular relationships between arthropod-borne microbiota and their vectors as studied by various approaches, including arthropod tissue culture and electron microscopy.

Various aspects, particularly immunology and microbiology, of selected infectious diseases are under investigation. Scrapie and progressive pneumonia of sheep, and Aleutian disease and encephalopathy of mink are studied as models of chronic degenerative diseases of man. Limited studies are made on rabies, tularemia, and the PLT group of organisms. More basic inquiries are made into fundamental mechanisms in delayed hypersensitivity and antibody production according to immunoglobulin class.

The fractionation of microbial agents, such as *Mycobacteria, Bordetella,* and Gram-negative organisms, by special biophysical and biochemical methods and the role of these subcellular fractions in immunity, hypersensitivity and other host responses are subjects of major investigations.

Opportunities for training associated with these research projects are provided in comparative pathlogy, electron microscopy, virology, immunology, immunochemistry, and a wide variety of specialized biophysical and biochemical methodology.

National Institute of Arthritis and Metabolic Diseases

J. E. Rall, M.D., Ph. D., Director of Intramural Research

Robert S. Gordon, Jr., M.D., Clinical Director

Clinical Associates

The NIAMD appoints approximately ten Clinical Associates each year. The assignments are for 2 years and ordinarily are not extended. A single position of Senior Associate is open each year and is ordinarily filled from among Clinical Associates during their second year in NIAMD.

Each Clinical Associate is attached for his 2-year duty period to one of the clinical branches or sections, within which he carries out both clinical work and laboratory studies. He is, in effect, an apprentice clinical investigator, working both on the wards and in the laboratory under the guidance of an experienced preceptor. The Associate is encouraged to choose his own problem for independent investigation, subject to the limitation that the facilities required for its successful pursuit, and the technical advice and supervision necessary, must be available to the branch or section in which he is to be working. In addition, he provides professional care for the research patients admitted to the service of his branch chief, and assists in the work of that branch in the outpatient department. There is considerable variation among the branches of NIAMD with respect to the proportion of the Associate's time required for patient care activities.

Since appointments are for 2 years, vacancies do not necessarily occur within each program area each year. The chiefs of branches or sections having openings for new Clinical Associates, and the Clinical Director, screen applications and select candidates for personal interviews. After interviews are completed and the results of matching are announced, each successful candidate is asked to confirm his acceptance of the position with which he was matched. It is not possible, after this, to change the Associate's assignment within NIAMD.

The list below identifies all of the clinical research branches within NIAMD, and their sections, by title and by the name of the chief. The Program Area Selection Check List indicates those having vacancies to be filled at this time. Prospective applicants who are not familiar with the qualifications and research accomplishments of the branch and section chiefs, or with the details of their current investigative and clinical programs, are encouraged to write Dr. Robert S. Gordon, Jr., Clinical Director, NIAMD, Building 10, Room 9N–222, Bethesda, Md. 20014.

Supplementary information sheets on each branch, together with selected bibliographic citations, are available on request.

Clinical Associate in Experimental Pathology

In addition to Clinical Associates who take care of patients on wards in the Clinical Center, the Laboratory of Expermiental Pathology has clinical responsibility for surgical and autopsy material. This Laboratory appoints approximately two Clinical Associates in Experimental Pathology each year. Further information can be obtained from Dr. Gert L. Laqueur, Chief of the Laboratory of Experimental Pathology.

Staff Associate in Epidemiology

One or two candidates are chosen each year for a 2-year assignment studying the epidemiology of chronic disease (diabetes, arthritis, cholelithiasis, etc.) among the Pima Indians of Arizona. The Associateships begin after internship, and a CORD deferment is not necessary. Candidates interested in this possibility are encouraged to write Dr. Peter H. Bennett, Epidemiology & Field Studies Branch, NIAMD, 4747 No. 16th St., A-147, Phoenix, Ariz. 85016, for more detailed information.

Research Associates

The National Institute of Arthritis and Metabolic Diseases has four positions available each year for Research Associates. These 2-year appointments, usually beginning on July 1, are designed to give highly qualified physicians an opportunity to improve their backgrounds for careers in basic medical research. During his stay here, each Research Associate will devote the larger part of his time to participation in laboratory research under the immediate supervision of a preceptor. The chosen candidates are free to choose a preceptor (upon mutual agreement) in any area in the Institute, either clinical or basic research. Should he elect a clinical area, he would not participate in clinical care of patients. The Research Associate, approximately 1 year prior to beginning, will visit NIAMD to select the laboratory and preceptor with whom he wishes to work. Candidates desiring further information about the laboratories, staff and bibliography of NIAMD may obtain this by writing to Dr. J. E. Rall, Director of Intramural Research, NIAMD, National Institutes of Health, Bethesda, Md. 20014.

Clinical Research Branches

Arthritis and Rheumatism Branch—Dr. John L. Decker

Section on Connective Tissue Disease—Drs. John L. Decker, Henry Metzger, Paul Plotz, Peter Goldman, and Alfred D. Steinberg

Clinical Endocrinology Branch—Dr. Jacob Robbins

Section on Diabetes and Intermediary Metabolism—Drs. Jesse Roth and Phillip Gorden

Section of Endocrine Biochemistry—Drs. Jacob Robbins, Jan Wolff, Saul Rosen, Hans Cahnmann, Harold Edelhoch, and Charles Lewallen

Clinical Hematology Branch—Dr. N. Raphael Shulman
Digestive and Heredity Diseases Branch—Dr. Leonard Laster
Metabolic Diseases Branch—Dr. Robert S. Gordon, Jr.
Section on Mineral Metabolism—Dr. Gerald D. Aurbach
Section on Physiology and Clinical Nutrition—Dr. Robert S. Gordon, Jr.
Section on Liver Diseases—Chief to be appointed
Section on Diseases of the American Indian—Dr. Scott M. Grundy
Pediatric Metabolism Branch—Dr. Paul A. diSant'Agnese

Basic Research Laboratories

Mathematical Research Branch—Dr. John Z. Hearon
Laboratory of Nutrition and Endocrinology—Dr. Herbert Sober
Section on Nutritional Biochemistry—Dr. John G. Bieri
Section on Endocrinology—Dr. Robert O. Scow
Section on Vitamin Metabolism—Dr. Bernard Kaufman
Section on Developmental Biochemistry—Dr. Herbert Sober
Section on Membrane Regulation—Dr. Martin Rodbell

Laboratory of Biochemistry and Metabolism—Dr. G. Gilbert Ashwell
Section on Enzymes and Cellular Biochemistry—Dr. William B. Jakoby
Section on Intermediary Metabolism—Dr. Yale J. Topper

Laboratory of Experimental Pathology—Dr. Gert L. Laqueur
Section on Histochemistry—Dr. George G. Glenner
Section on Chemical Pathology—Dr. Vincent Marchesi
Section on Biophysical Histology—Dr. Ned Feder
Section on Rheumatic Diseases—Dr. Leon Sokoloff

Laboratory of Biochemical Pharmacology—Dr. Herbert Tabor
Section on Pharmacology—Dr. Herbert Tabor
Section on Biochemistry—Dr. Victor Ginsburg
Section on Biochemistry of Amino Acids—Dr. Simon Black

Laboratory of Chemistry—Dr. Bernhard Witkop
Section on Carbohydrates—Dr. Hewitt G. Fletcher, Jr.
Section on Medicinal Chemistry—Dr. Everette L. May
Section on Steroids—Dr. Yoshio Sato
Section on Biochemical Mechanisms—Dr. Louis A. Cohen
Section on Metabolites—Dr. Bernhard Witkop
Section on Microanalytical Services and Instrumentation—Dr. David Johnson
Section on Pharmacodynamics—Dr. John W. Daly

Laboratory of Physical Biology—Dr. John B. Buck
Section on Comparative Physiology—Dr. John B. Buck
Section on Cellular Physics—Dr. Richard J. Podolsky

Laboratory of Chemical Physics—Dr. Edwin D. Becker
Section on Molecular Biophysics—Dr. Edwin D. Becker
Section on Electrochemistry & Colloid Physics—Dr. Karl Sollner
Section on Physiology—Dr. Paul Altland

Laboratory of Molecular Biology—Dr. H. Todd Miles
Section on Metabolic Enzymes—Dr. Martin Gellert
Section on Molecular Genetics—Dr. Jun-ichi Tomizawa
Section on Physical Chemistry—Dr. Gary Felsenfeld
Section on Molecular Structure—Dr. David R. Davies
Section on Microbial Genetics—Dr. Robert Martin
Section on Organic Chemistry—Dr. H. Todd Miles
Section on Theoretical Molecular Biology—Dr. Terrell Hill

Laboratory of Chemical Biology—Dr. Christian B. Anfinsen
Section on Biosynthesis and Control—Dr. Robert F. Goldberger
Section on Protein Chemistry—Dr. Christian B. Anfinsen

Laboratory of Biophysical Chemistry—Dr. Koloman Laki
Section on Bioenergetics—Dr. David Kominz
Section on Macromolecules—Dr. Harry A. Saroff
Section on Physical Biochemistry—Dr. Koloman Laki

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National Institute of Child Health and Human Development

Gerald D. LaVeck, M.D., Director

Charles U. Lowe, M.D., Scientific Director

This Institute offers associate training programs in the branches indicated below. These programs include activities appropriate to a variety of specialized backgrounds, including obstetrics and gynecology, pediatrics, neonatology, internal medicine and psychiatry, as well as physiology, biochemistry, biophysics, reproductive physiology, genetics, pharmacology, psychology, and developmental biology.

The Behavioral Biology Branch (Phillip G. Nelson, M.D., Ph. D., Chief). Conducts electrophysiologic and biochemical studies of the neurobiologic basis for short- and long-term interaction between nerve cells. The central neural mechanism underlying sensory discrimination in primates is studied by electrophysiologic and behavioral techniques.

The Section on Brain and Behavior (David Symmes, Ph. D., Head). Electrophysiologic correlates of sensory coding and discriminative behavior are analyzed using microelectrode computer techniques. Behavioral consequences of brain lesions are studied.

The Section on Neurobiology (Phillip G. Nelson, M.D., Ph. D., Head). Tissue cultured neural and muscle tissue and small *in vitro* vertebrate and invertebrate neural systems are studied electrophysiologically and biochemically. Long-term interactions between neurons and between nerve and muscle are of particular interest.

Developmental Biology Branch (Charles U. Lowe, M.D., Acting Chief). In this unit the normal and abnormal developmental aspects of cellular differentiation, tissue interaction and morphogenesis are investigated with the methods and within the conceptual framework of such disciplines as developmental biology, developmental pharmacology, experimental embryology and the development of behavior. Current studies include investigations of the role of masked messenger RNA in induction and the developmental phenomenon of "determination" and studies of differentiation and organogenesis.

Developmental Immunology Branch (John B. Robbins, M.D., Chief). In this new program of the Institute the development of immunity in infants and children is being studied utilizing *Hemophilus influenzae* type b disease and its type b capsular polysaccharide as a model system. The immunogenic characteristics of the type b polysaccharide and its protective value following immunization of infants and children

is being studied in a field trial. Investigations into the nature of a serologic relation between cell surface structure and type b polysaccharide in individuals with *Hemophilus influenzae* disease are being conducted to study the susceptibility of non-immune individuals.

Particular emphasis is currently being directed toward establishing the relation between enteric organisms found to possess the cross reacting antigens to *H. influenzae* type b and the development of "natural" immunity to diseases caused by this pathogen.

Current plans project an obstetric and newborn delivery program at the Clinical Center. This program will provide an opportunity to study normal perinatal and neonatal adaptation to the antigens of the nasopharyngeal and enteric microorganisms.

Gerontology Research Center (Nathan W. Shock, Ph. D., Associate Scientific Director for Gerontology). The multidisciplinary program of the Center, located in a special research building on the campus of the Baltimore City Hospitals, offers Clinical (primarily clinical research) and Staff (primarily basic research) Associate training. Preference is given to candidates who intend to pursue careers in investigative and academic medicine. With appropriate approval, Associates may participate in clinical activities of the Baltimore City Hospitals and the nearby hospitals of the Johns Hopkins University and the University of Maryland. The Baltimore City Hospitals are affiliated with both institutions.

Associates participate in a seminar conducted by the staff of the Center which presents a comprehensive view of research in aging. Weekly research conferences are presented by members of the staff and invited lecturers.

In support of the programs in molecular aging and cellular and comparative physiology the Center maintains extensive animal colonies to provide rats, mice, hamsters, house flies, campanularia, rotifers, etc., of known ages, including senescent animals. Animal operating rooms are available as well as shops for the design and construction of special equipment. The library of the Center includes standard scientific journals as well as an extensive collection of the literature on aging research.

The Gerontology Research Center is composed of four branches:

Laboratory of Cellular and Comparative Physiology (Bertram Sacktor, Ph. D., Acting Chief). This Laboratory studies biochemical, physiological, and morphological changes in cells and tissues of animals of different species during aging. Special program emphasis is placed on studies relating aging to immunologic phenomenon. The effects of environmental factors on mortality and life span are measured and the biological mechanisms established. Age changes in the ultrastructure (electron microscopy) and function of tissues are correlated.

Clinical Physiology Branch (Reubin Andres, M.D., Chief). This Branch is primarily concerned with studies on physiological changes occurring during the entire adult age span. Studies include quantitation

of age changes, elucidation of mechanisms underlying these changes, and the relation between aging processes and specific disease states. Clinical research is conducted on 600 community-dwelling volunteers who comprise a panel for an extensive longitudinal study of human aging. They spend 2½ days every 18 months on the Gerontology Research Ward in the adjoining Baltimore City Hospitals.

The Endocrine Section (Robert I. Gregerman, M.D., Chief) conducts studies in (a) thyroid hormone physiology and especially the kinetics of hormonal release, transport and action and (b) renin and angiotensin physiology.

The Cardiovascular Section (Nathan W. Shock, Ph. D., Acting Chief) investigates cardiovascular hemodynamic function in man using non-invasive methods and in the rat and dog by a variety of experimental techniques.

The Metabolism Section (Reubin Andres, M.D., Chief) conducts research on the kinetics of glucose homeostasis and related endocrine functions using a servo-control technique for clamping glucose levels in man.

The Human Performance Section (Arthur H. Norris, M.S., Chief). This Section is responsible for a wide variety of studies on age changes in body composition, pulmonary and exercise physiology, and neuromuscular function.

Laboratory of Behavioral Sciences (Bernard T. Engel, Ph. D., Chief). This program includes studies of the effects of aging on motor behavior, perceptual skills, learning, memory, problem-solving ability, and personality characteristics. There are also studies on the interrelationships among aging and autonomic responses, and the clinical applications of voluntary autonomic control are being investigated. Laboratory facilities exist for measuring cognitive and perceptual functions in man; psychophysiological responses in man; learning and motor behavior in rodents (including selected in-bred strains of mice); learning, cardiovascular and neuropsychological responses in monkeys.

Laboratory of Molecular Aging (Bertram Sacktor, Ph. D., Chief) conducts research on the biochemical control systems in enzyme action and metabolism and on the regulatory processes in molecular biology, with reference to adult development and aging. Studied are mechanisms for regulating glycogenolysis, glycolysis, gluconeogenesis, citric acid cycle activity, and oxidative phosphorylation; transport of sugar, metabolites and ions; action of hormones in regulating intermediary metabolism; enzyme induction and the biogenesis and turnover of cellular membranes and organelles. Investigated also are the primary and conformational structures of DNA and RNA; the interactions of polynucleotides with each other, metal ions and proteins; cellular uptake of synthetic polynucleotides; polynucleotide hybridization; and the expressions of these interactions in terms of biological function. Correlations between physical

properties, chemical composition, structure, and function of connective tissues, blood vessels and skin are established during the aging process.

The Laboratory of Biomedical Sciences (J. C. Robinson, M.D., Ph. D., Chief) conducts basic research in developmental enzymology, intermediary metabolism, physiological control, developmental pharmacology, and molecular structure.

In the Section on Developmental Enzymology (J. C. Robinson, M.D., Ph. D., Head) primary interest centers on the identification and characterization of pregnancy-associated maternal blood plasma enzymes and proteins, the characterization of enzymes synthesized by the placenta, and an analysis of some of the factors involved in enzyme induction in the developing fetus.

Section on Intermediary Metabolism (Gordon Guroff, Ph. D., Head). This Section is involved in the development of laboratory analogs of mental retardation through the use of specific chemical agents and enzyme inhibitors, in the investigation of screening procedures for enzyme defects in mental retardation, and in the evaluation of the effects of excesses or deficiencies of intermediary metabolites on cellular differentiation and organogenesis. Other studies concern the biosynthesis and degradation of macromolecules in neural tissue, the transport of small molecules across cellular membranes, and the mechanism of action of enzymes of neurochemical interest. The overall efforts of the Section are to understand how changes in specific enzymes lead to changes in the behavioral patterns of the whole animal.

The Section on Physiological Controls (Walter H. Glinsmann, M.D., Head) is concerned with hormonal, neurotransmitter, and substrate regulation of cell function and biochemical differentiation. Current studies focus on enzymatic mechanisms controlling hepatic glucose output, substrate and hormone-dependent induction of enzymes in embryonic and adult liver, mode of action of biogenic amines, and neuroendocrine regulation of indole metabolism in the pineal gland.

Section on Developmental Pharmacology (Daniel W. Nebert, M.D., Head) investigates the macromolecular processes involved in the induction of pharmacologically important enzymes by drugs, aromatic hydrocarbons, insecticides, or hormones. The Section also investigates the transplacental effects of these environmental stimuli on microsomal enzyme activity, on the metabolism of endogenous substrates in fetal tissues, and on normal fetal growth and development. *In vivo* and *in vitro* methods, including cell culture, are used to study pharmacogenetic defects in mammalian cells.

Section on Molecular Structure (Erhard Gross, Ph. D., Head) emphasizing laboratory automation, develops and applies fundamental methods for the structural elucidation and synthesis of biologically significant molecules. It is also engaged in the isolation and characterization of cell organelles, such as lysosomes of placental origin, and aims at the

identification of regulatory processes operative during pregnancy. The Section establishes structure-function relationships of enzymes and of physiologically active peptides of low molecular weight. Broadly based studies seek to correlate the presence of unusual amino acids in novel types of peptide structure with their action on the fetoplacental unit.

Laboratory of Molecular Genetics (Philip Leder, M.D., Chief) is concerned with both the biochemical and physiologic aspects of the hereditary process. Current studies involve the use of bacteria and their viruses, as well as certain mammalian viruses, as model systems for the investigation of information flow from gene to messenger to protein. Emphasis is on the mechanism of protein biosynthesis, molecular aspects of immunogenesis, and the regulatory genetics of the virus lambda.

Pregnancy Research Branch (Ronald Chez, M.D., Chief) conducts research in the physiology of pregnancy, the effects of disease states on pregnancy, and the identification of those factors which increase perinatal and maternal morbidity and mortality. At this time studies are primarily oriented toward the use of pregnant baboons, Rhesus monkeys, and sheep as models for human application. The interrelationships of fetal, placental, and maternal polypeptide hormone metabolism, tests of placental function and reserve, and the rate limiting influences on sex steroid production during pregnancy are being examined.

The Branch is beginning a clinical research program with both outpatient prenatal and postpartum clinics and inpatient prenatal and labor and delivery facilities. Methods for monitoring the progress of labor and delivery will be studied.

Reproduction Research Branch (Mortimer B. Lipsett, M.D., Chief) conducts an integrated program of clinical, biochemical and biologic studies pertinent to reproductive biology and endocrinology. Studies of the gonadotropic hormones range from separation and analysis, correlation of molecular structure with metabolism and function, to synthesis *in vitro,* and mode of action. The broad aspects of sex steroid hormone metabolism remain a focus of interest and are being explored *in vitro* and *in vivo*. The human and the Rhesus monkey are used to investigate ovaluation, the menstrual cycle, control of corpus luteum function, and pregnancy. Among the specialized techniques in current use are: radioimmunoassay for protein hormones, radioligand assays for steroid hormones, tissue culture, and protein separative and analytic procedures such as polyacrylamide gel electrophoresis and isoelectric focussing, and cytogenetics.

The Branch staffs a general endocrinology clinic with special emphasis on problems involving the pituitary gland, adrenal cortex, gonads, growth and development. Infertility clinics for men and women are a source of patients for clinical studies. For their first year, assignments of Clinical Associates are shared between the ward and laboratory; the

second year is spent primarily in the laboratory. The Clinical Associate works in a research area under the guidance of a Senior Investigator.

The Social and Behavioral Sciences Branch (Leon J. Yarrow, Ph. D., Chief) engages in studies of cognitive, social and personality development in the early years of life. Current studies center around early environmental influences on development, and are concerned with both methodological and theoretical issues. Research in progress is on the relations between specific aspects of early mother-infant interaction, e.g., sensory-perceptual stimulation, social-affectional components of maternal behavior and early cognitive, motivational and social development. Studies are underway to assess early father-child interactions and their impact on the development of boys and girls. Other research is concerned with reciprocal influences in mother-infant interaction, the ways in which the infant influences maternal behavior. This research involves the development of techniques for assessing basic individual differences in infant characteristics, e.g., activity level, vulnerability to stress; and procedures for analyzing mother-infant interactions as a dyadic unit. Studies of preschool children in school environments deal with several interrelated problems: development of methods for analyzing the complex learning environments of preschool children; study of the influence of various types of teacher behavior, and sensory stimulation on cognitive and personality functions.

National Institute of Dental Research

Richard C. Greulich, Ph. D., Director of Intramural Research

George E. Garrington, D.D.S., Deputy Director of Intramural Research (Clinical Investigations)

The National Institute of Dental Research conducts research programs in laboratory, clinical and applied science, germane not only to dental health but also to the broader interests of biology and medicine.

Physicians are appointed for a 2-year period to the Institute's laboratory or clinical programs as Research or Clinical Associates. In general, three Research Associate and two Clinical Associate positions are available annually. Specific program areas, however, will not necessarily have vacancies for Associates in a particular year.

For the most part, dentists will be appointed for 2 years as Dental Clinical Associates, with a dual commitment to research and service as described on page 2. Three or four Dental Clinical Associates will be selected annually. Dental graduates who possess specialized training and interests applicable to a particular research program of the Institute may also be considered for appointment as Staff Associates, with a full-time assignment to the appropriate laboratory or branch. The number of positions of this type to be filled will be determined solely according to programmatic need, and will usually not exceed two per year.

Brief descriptions of the program areas to which Associate appointments are made are provided in the following paragraphs. Additional information about specific programs may be obtained upon request to the Director of Intramural Research, NIDR, National Institutes of Health, Bethesda, Md. 20014.

The Laboratory of Biochemistry (Karl A. Piez, Ph. D., Chief) conducts programs in basic research covering a broad range of biochemical topics. The laboratory has as its objective the investigation of fundamental biochemical processes in normal and disease states.

Research and Staff Associates are assigned to one of four sections according to the interest of the Associate: Protein Chemistry (Karl A. Piez, Ph. D., Chief), Connective Tissue Chemistry (George R. Martin, Ph. D., Chief), Enzyme Chemistry (John E. Folk, Ph. D., Chief), or Cell Biology (Herbert L. Cooper, M.D., Chief). Ample opportunity is provided for interchange and collaboration between sections and with other groups at NIH.

Current research includes: chemical and physical chemical studies on proteins; the chemistry of crosslinks and the determination of amino acid sequences in collagen; the biosynthesis of collagen, elastin and other connective tissue components in animals and in tissue culture; the

chemistry and mechanism of action of enzymes; the macromolecular events occuring in the cell prior to and during differentiation; and the chemistry and mechanism of action of muscle proteins.

The Laboratory of Microbiology (Stephan E. Mergenhagen, Ph. D., Chief) has as its broad objective the elucidation of the microbial ecology of the oral cavity, that is, to understand the interactions of members of the oral microbiota with one another and with the tissues of the host in which they reside, particularly in reference to oral and systemic health and disease. The broad basic programs in microbiology have application to medical and dental problems. Cooperative research with other laboratories is conducted as required by the interdisciplinary nature of particular projects.

The Virology Section (Abner Louis Notkins, M.D., Chief) is interested primarily in factors responsible for recurrent and persistent virus infections. Studies are being conducted on the effect of virus infections on the functional capacity of the immune system; the mechanism of neutralization of sensitized herpes simplex virus by antiviral antibody, antigamma globulin and the purified components of complement; factors responsible for the persistance of infectious virus and elevated enzymes in mice infected with lactic dehydrogenase virus; and cell fusion as a method for recovering infectious virus.

The Microbial Physiology Section (Charles L. Wittenberger, Ph. D., Chief) conducts research on mechanisms by which growth and biochemical activities of microbial cells are regulated, with a view to explaining physiological phenomena in molecular terms. Current studies are directed toward resolving the means by which lactic acid production by cariogenic streptococci is regulated. The pathways by which various organic compounds are fermented by this group of organisms is also being explored. In addition, comparative investigations on the genetics and metabolic activities of microorganisms are being pursued as part of a general approach to systematic microbiology.

The Immunology Section (Joost J. Oppenheim, M.D., Chief) is primarily involved in studies on the role of immunological mechanisms in oral and systemic disease. Current investigations are concerned with the immunobiological effects of endotoxins and other toxic products of microorganisms implicated in periodontal disease. The role of serum complement and "natural" antibodies in endotoxin-induced inflammation is being explored. Effects of lactic dehydrogenase virus and other adjuvants on immunological tolerance and the mechanism of tolerance at the cellular and subcellular level are being investigated. Studies are being carried out on immunosuppressive agents such as antilymphocyte serum and its mechanism of action in transplantation reactions.

The Laboratory of Biological Structure (Marie U. Nylen, D.D.S., Chief) is primarily concerned with structural parameters of normal and abnormal function as expressed at varying levels of bio-

logical organization, ranging from the subcellular to the organismic. Information is adduced from the application of biophysical and chemical methods, techniques of experimental embryology, as well as from relevant tools of modern histology.

Research and Staff Associates are appointed to the Laboratory and are assigned by mutual agreement to a preceptor in one of the following sections; Molecular Structure (E. D. Eanes, Ph. D., Chief); Experimental Pharmacology (C. T. G. King, Ph. D., Chief); Structural Interactions (H. A. Bladen, Ph. D., Chief); and Experimental Morphology (M. U. Nylen, D.D.S., Chief).

Currently, the Laboratory is engaged in a broad series of structurally oriented projects. These relate to normal growth and differentiation, drug-induced developmental abnormality, the secretory process, crystal chemistry, and mineralized tissues, as well as to morphofunctional characteristics of whole and fractionated tissue cells, macromolecules, microorganisms and viruses. Opportunities for cooperative research and training are offered in electron microscopy and diffraction, contact and projection microradiography, X-ray diffraction, infrared absorption spectrophotometry, and cytochemistry.

The Institute's Environmental Mechanisms Section and Neural Mechanisms Section execute research programs broadly focusing on oral homeostatic mechanisms in health and disease. Emphasis is currently being placed on (1) the microbial ecology of the mouth; (2) integrated responses of the oral system as mediated by neural control; and (3) development of techniques for utilizing computer systems in experimentally monitoring and regulating the multiparametric factors which contribute to oral homeostasis. Experimental approaches derived from the disciplines of biochemistry, physiology, computer sciences and electronics play an essential role in these studies.

Specifically, the Environmental Mechanisms Section (Micah I. Krichevsky, Ph. D., Chief) investigates systems of controlled and uncontrolled interactions between a cell or group of cells and its environment. A primary aspect of these studies relates to the role of environmental cyclic or acyclic mononucleotides in cell interactions, especially those resulting in growth, chemotaxis, or structural differentiation.

Also under investigation is the response of caries-conducive streptococci to environmental parameters. Presently under study are: the dynamics of growth of these bacteria; their minimal nutritional requirements; the sequestration of phosphate (a main constituent of teeth) into the bacterial cell substance; the determinants of acquisition of capability of streptococci to adhere to surfaces; and, related to this last, the dynamics of accumulation of cell-associated polysaccharides.

The Neutral Mechanisms Section (Ronald Dubner, D.D.S., Ph. D., Chief) conducts research on neural mechanisms in the oral and facial regions, especially those related to responses of the organism to its ex-

ternal environment. Current research topics include (1) peripheral and central neural mechanisms of orofacial sensation mediated by the trigeminal system, with particular emphasis on responses to tactile and noxious stimuli, and (2) sensory interaction in association areas of the cerebral cortex and the role of these cortical sites in higher cognitive functions of the brain. These research activities utilize conventional neurophysiological techniques of recording the electrical activity of individual cells in the brainstem and cerebral cortex and computer analysis of the temporal patterns of single-cell activity evoked by different somatic and visual stimuli. In addition, ultrastructural studies of the trigeminal brainstem nuclei are conducted in conjunction with neurophysiological studies of the trigeminal system.

The Experimental Pathology Branch (Richard C. Greulich, Ph. D., Acting Chief) conducts basic and applied research on a variety of diseases, especially those of major interest to dentistry. Metabolic studies of connective tissues hold a special interest.

The Histochemistry Section (William A. Gibson, D.D.S., Acting Chief) conducts histochemical, microchemical, biochemical and tissue culture studies of various oral and other tissues. Current studies include (1) the isolation, purification and characterization of collagenase from several sources, (2) the relation of collagenase, proline hydroxylase, and cross linking enzyme levels to various oral dieseases, (3) the relation of hyaluronidase, beta glucuronidase, and beta glucosaminidase levels to oral diseases, (4) histochemical studies of bone resorption, developing teeth and of various oral disease conditions, and (5) studies of factors in the oral environment that promote degradation of the oral tissues in periodontal diseases.

The Diagnostic Pathology Section (Howell Archard, D.D.S., Chief) is concerned with the operation of a diagnostic oral pathology service. An accredited residency training program in oral pathology is also offered.

The Experimental Oncology Section (James E. Hamner III, D.D.S., Ph. D., Chief) is concerned with histopathologic studies of oral disease in man and in animals. Current studies include histopathologic studies of tissue reactions to synthetic implants, and experimental oral tumors in animals.

The Human Genetics Branch (Jerry D. Niswander, D.D.S., Chief) conducts projects in experimental, clinical, and population genetics, with the objective of elucidating the genetic mechanism in various diseases and normative traits. A variety of approaches ranging from biochemical to mathematical as well as clinical skills in both medicine and dentistry are utilized. The program of the branch is implemented by two sections.

The Developmental Genetics Section (Kenneth S. Brown, M.D., Chief) studies normal and abnormal traits of man and experimental

animals with a view to determining the nature of the developmental processes involved, and the degree to which these are under genetic control. Experimental embryology is used to determine the nature of developmental processes that result in structural variations of the face and dentition. Morphologic anomalies of the dentition are studied histologically in combination with breeding experiments. Variation in human taste and smell perception is investigated to determine the nature of the receptor processes and their degree of genetic control.

The Population Genetics Section (Jerry D. Niswander, D.D.S., Chief) conducts field and laboratory studies of congenital malformation, malocclusion, and dental variation in different populations. Microdifferentiation in human populations (particularly American Indian groups) is also a major area of concern. Investigations include the effects of natural selection and inbreeding, as well as other factors affecting mating pattern on the genetic structure and disease patterns of different groups. A major source of data for this work is obtained from red cell and serum typing conducted within the Branch.

The Disease Prevention and Therapeutic Branch (James P. Carlos, D.D.S., Chief) is concerned with the study of the occurrence of oral diseases in relation to various characteristics of the persons examined, their way of life, and the environment in which they live. Field studies are designed and conducted in an effort to identify, within this dynamic complex, variables which influence favorably or unfavorably the occurrence of disease. The objective of epidemiological study is to provide information that might prove useful in the prevention, control or treatment of disease.

Research activity of the Branch is currently devoted to the epidemiological study of dental caries, periodontal disease, and occlusion, which represent by far the 3 most prevalent problems of oral health. Work is undertaken collaboratively within the Branch, and usually also involves participation of other units of the Institute, especially the Dental Services Branch.

In connection with the National Caries Program of NIDR, the Branch is heavily engaged in a program of clinical and field trials of agents and techniques with anti-caries potential.

The Clinical Trials Section (H. R. Englander, D.D.S., Chief) is engaged in *in vitro* and animal investigations of the causation of dental caries and periodontal diseases, and of agents with preventive and therapeutic potential.

The Biometry Section (James P. Carlos, D.D.S., Chief) provides statistical and data processing consultation to Institute and other dental scientists, and conducts a research program in the methodology of design and analysis in oral research.

Investigations presently being conducted by the Branch are especially concerned with: (1) the role of dental plaque in the causation of dental

caries and periodontal disease; (2) evaluation of new therapeutic measures directed against caries and periodontal disease; (3) assessment of the prevalence and severity of malocclusion in terms of newer epidemiological methods of diagnosis and scoring; and (4) improvement in statistical and clinical methodology in dental research.

The Oral Medicine Branch (Edward A. Graykowski, D.D.S., M.D., Chief) provides the specialty staff for the conduct and support of clinical investigations, both inpatient and outpatient, relating to oral disease. Etiologic and therapeutic investigations are wide-ranging, with particular stress being placed upon interrelationships of oral and systemic disease. The Branch is uniquely suited to the study of such interrelationships because of the wide variety of interests reflected among its physician, dentist, and allied health professional personnel. The following items are briefly illustrative of some current investigative programs.

Salivary gland studies are presently concentrated upon the effects of Sjögren's syndrome. Efforts are also being directed toward determining the potential of salivary gland structure and function as well as of saliva itself as diagnostic tools. Similarly, the glands and their products are being examined with reference to their potential for monitoring the progression of disease and of the efficacy of therapy.

Laboratory and clinical investigations of serum protein structure and behavior are employed in the study of connective tissue disorders such as Behcet's syndrome, scleroderma, systemic lupus erythematosus, and Sjögren's syndrome. Emphasis is also being directed toward the study of rheumatoid arthritis as it may affect oral function via temporomandibular joint involvement.

Dental transplantation is studied principally from the standpoint of immunologic considerations, and emphasizes the development of techniques which will minimize homograft rejection. Corollary studies of host response to non-antigenic materials of interest as potential dental implants (including metals, ceramics and organic polymers) are also in progress.

The Oral Pharyngeal Development Section (James F. Bosma, M.D., Chief) is concerned with investigations of the development of form and of respiratory and feeding functions in normal and in impaired infants and children. Study methods commonly include standard and cephalometric roentgenography, cinephotography, and speech recording. Basic anatomic studies are an integral part of the work of this section. Particular efforts are made to adapt familiar study techniques and therapies to patients severely handicapped by anomaly or by neurologic impairment.

The Dental Services Branch (Samuel Kakehashi, D.D.S., Chief) has as its prime function the dual responsibility of providing dental care to the NIH-wide research patient population as well as of providing facilities and supportive activity to all intra-Institute clinical programs.

This patient exposure provides a unique opportunity for gaining experience in the observation, treatment, and study of orofacial problems related to a variety of systemic disease. All Dental Clinical Associates are assigned to this Branch administratively so as to facilitate their service-related activities. However, an individual program is arranged for each Associate in order that he may also pursue effectively his clinical and/or basic research interests.

National Institute of Environmental Health Sciences

David P. Rall, M.D., Ph. D., Director

William W. Payne, Sc. D., Deputy Director

General

The mission of the National Institute of Environmental Health Sciences (NIEHS) is to identify the chemical, physical, and biological, factors in the enviroment that can adversely affect man; to contribute to an understanding of the mechanisms and manifestations of human diseases produced by these agents; and to provide the scientific basis for the development of control measures by other agencies. NIEHS is particularly concerned with the effects of agents at low concentrations acting over long periods; the interaction of multiple agents resulting in enhanced effects; and the modifying effects of variable physical and biological states within man on susceptibility to and course of disease induced by these agents.

There is no single discipline that is unique or specific for the study of environmental health problems. Rather, the distinctive requirement for such research involves the application of a spectrum of skills including biology, biochemistry, bioengineering, biometry and epidemiology, chemistry, pathology, pharmacology, physics, toxicology, and veterinary sciences.

Location

The headquarters and intramural research programs of NIEHS are located at the National Environmental Health Sciences Center (NEHSC) in Research Triangle Park, N.C. The National Institute of Environmental Health Sciences is the only one of the 10 Institutes comprising the National Institutes of Health to be locaed away from the Bethesda, Md., campus.

Proximity to three universities—the University of North Carolina at Chapel Hill, Duke University at Durham, and North Carolina State University at Raleigh—has encouraged the development of a close working relationship between the staffs of the universities and the Institute. This relationship affords the NIEHS staff access to extensive library facilities as well as opportunities to participate in teaching, in seminars, and in other scientific and professional activities associated with the universities.

Staff Associates

Staff Associates will work at the National Environmental Health Sciences Center under the direction of Dr. David P. Rall, Director, and a Branch Chief in the Institute. Each Associate will work directly under a senior scientist in an area of research chosen by the Associate and the Institute.

The Analytical and Synthetic Chemistry Branch (Lawrence Fishbein, Ph. D., Chief) supports programs designed to conduct and augment research related to the effects of a broad spectrum of environmental agents (pesticides, food additives and contaminants, trace metals, and pollutants of air and water—including also their metabolic and degradation products). The program also includes the elaboration of environmental parameters (ultraviolet, ozone, and thermal) on the stability of diverse pesticides and related derivitives; the analysis of multiple components in the elaboration of synergistic effects; the development or improvement and standardization of analytical techniques for the determination of specific chemicals; and the preparation of required intermediates for confirmation of identity of metabolites and degradation products through synthetic procedures. Research studies by the Branch include the separation and identification of components of essential oils, the study of biliary and urinary metabolites following administration of pesticide synergists and other toxicants, and the determination of the effects of aflatoxin excreted in the milk of rats on the development of their offspring.

The Animal Science and Technology Branch (John A. Moore, D.V.M., Chief) is responsible for the acquisition, quarantine, and conditioning of all biological models for the NIEHS; for the maintenance, husbandry, and veterinary care of all experimental colonies utilized by the Institute. Individual staff scientists of the Animal Science and Technology Branch (ASTB) represent such diverse professional disciplines as pathology, microbiology, hematology, clinical chemistry, and laboratory animal medicine. Current research programs that are consistent with the overall NIEHS mission include studies on the effect of chronic heavy metal exposure on immune competence; biological effects of phenoxy-acid herbicides on mammalian systems, and characterization of the toxic effect of tetrachlorodibenzo-p-dioxin.

The Cell Biology Branch (Robert G. Owens, Ph. D., Chief) seeks to clarify the long-range effects of noxious environmental agents on cells and tissues, to elucidate the fundamental mode of action of such agents, and to assess the significance of toxicant-induced malfunctioning after long-term exposure on the long-range health of man. Research currently underway includes investigation of the induction of mitochondrial defects by toxic agents, effects of alkylating and other types of environmental agents on metabolism and enzyme induction by xenobiotic compounds.

Important advances are being made toward characterizing the effects of toxins on ribosomes and on polysome integrity in relation to protein synthesis by use of mammalian tissue cultures and in animal models. The distribution and potential importance of mycotoxins in the environment are being explored. The fate and mode of action of toxins in the animal body are being studied along with the enzyme systems responsible for detoxifying foreign substances and eliminating them from the body. Chemical mutagenesis is recognized as an area of high priority in terms of national scientific need and a broad array of studies are in progress or will be organized. In addition to development of mammalian cell systems for evaluation of chemical mutagens, efforts include investigation of nucleic acid repair mechanisms, identification of genetic markers, and development of automated procedures to support population monitoring studies.

The Pathologic Physiology Branch (David P. Rall, M.D., Ph. D., Acting Chief) is concerned with the identification of environmental toxicants and the elucidation of their toxic mechanisms at the organ, cellular, and subcellular levels. Correlations are being sought between toxicant-induced changes in mammalian structure, as visualized by light and electron microscopy, and corresponding changes in function, as revealed by techniques of biochemistry and physiology. Work is in progress on the acute and chronic effects of the nervous and endocrine systems of a variety of chemicals and environmental pollutants, individually and in combination. Experimental lipidoses, and epilepsy, demyelination, and experimental thyroiditis are current areas of interest. The carcinogenic potential to the neonate marsupial of selected pesticides, heavy metals, and other agents is also under investigation. The marsupial is being utilized as a primary biological model in many of the studies underway.

The Pharmacology and Toxicology Branch (J. R. Fouts, Ph. D., Chief) studies the toxic effects on mammals of low level and/or chronic exposure to environmental constituents or contaminants. Interactions upon or within the animal of these environmental factors with each other and with drugs are also studied. Projects currently underway are evaluating some toxic effects of pesticides and heavy metals on some enzymes in excretory organs; detoxication mechanisms in liver, gut, and lung and effects of some chemicals and pesticides on these; accumulation of chemicals and drugs in various organs, especially lung, and process involved in these accumulations; synthesis of lung surfactant and effects of drugs and chemicals on this synthesis and release; effects of some model chemicals on pregnant animals and their offspring; effects of route of administration of chemical on toxic effects—especially the development of facilities and technics for administration of materials in vapor and aerosol form; species differences and age-related changes in effects of environmental toxic chemicals or agents. Extensive interaction of Pharmacology-Toxicology with Pathologic Physiology Branch and its pro-

grams in histology, histochemistry, and electron microscopy will occur, especially as these relate organ structure and ultrastructure with function.

Biometry Branch (David W. Gaylor, Ph. D., Chief). The mission of the branch is to provide biometrical support for the NIEHS program by employing mathematical and statistical techniques to determine the biological effects of chemical, physical, and biological agents present in the environment. This is accomplished by incorporating in the Institute program statistical principles of experimental design, sampling, and data analysis for both laboratory and epidemiological studies, as well as mathematical analyses of biological systems. Mathematical and statistical procedures are applied and, when necessary, developed to determine the distribution and to estimate the rates of environmentally related diseases among populations, test hypotheses and study the interactions of environmental agents from multi-factor laboratory experiments, and develop mathematical models for describing and predicting biological responses to environmental agents. Dose-response relationships are established from which threshold or acceptable doses may be predicted to aid in the establishment of control policies. The branch provides computing services for the processing of large sets of data and for the analyses of complex problems. In order to accomplish the mission of the Biometry Branch the following areas of activity are identified: (a) Analytical Statistics, (b) Statistical Epidemiology, (c) Mathematical Statistics, (d) Biomathematics, (e) Computer Programming, and (f) Data Processing.

Biophysics and Biomedical Instrumentation Unit, Research Services Branch (Lyle O. Thomas, Chief of Branch) provides for NIEHS the capability of studying the impact of physical factors in the environment on man's health. Some activities are conducted in collaboration with or in response to specific requirements of other programs within the Institute. Activities of the Unit include the investigation of the biological effects of physical factors alone or in combination with chemical and biological factors to which man may be exposed. Physical factors include but are not restricted to ionizing and non-ionizing radiation, heat, humidity, sound, and physical vibration. The Unit is also responsible for the development and improvement of research instrumentation to support its own mission as well as the total NIEHS program.

National Institute of General Medical Sciences

George J. Cosmides, Ph. D., Director

Pharmacology Research Associates

This Institute has eight to ten positions available each year for Pharmacology Research Associates. Those who are appointed begin on July 1 and will receive 2 years of postdoctoral training in a laboratory of a participating Institute of the National Institutes of Health under the Pharmacology Research Associate Training Program.

The program is directed to those who have already made a commitment in pharmacology by training or research in the field.

Associates will study principles of pharmacology and toxicology and the application of physical and chemical concepts to pharmacology. Training in such areas as applied mathematics, biometrics, organic chemistry, biochemistry, physics, and instrumentation is also available. During their tenure, Pharmacology Research Associates devote the larger portion of their time to laboratory research in the biomedical sciences, with no clinical responsibilities.

The purpose of this training is to develop leaders in pharmacology research for key positions in academic, industrial, and governmental research laboratories.

Professional growth is achieved through the process of personal guidance by senior NIH scientists, chosen by mutual selection, coupled with a variety of laboratory problems and many different research approaches, designed to advance both the work in progress and the competence of the prospective independent investigator.

Candidates who need experience in pharmacology and wish to broaden their experience in biomedical sciences may make their selection from the following program areas:

National Cancer Institute
- Laboratory of Chemical Pharmacology
  - Dr. Richard Adamson (drug metabolism)
  - Dr. Vincent Oliverio (biochemical pharmacology)
- Cancer Chemotherapy National Service Center
  - Dr. Abraham Goldin (chemotherapy)
- Laboratory of Physiology
  - Dr. Marco Rabinovitz (protein biosynthesis and antimetabolites)
- Chemistry Branch
  - Dr. C. Wesley Dingman (etiology of carcinogenesis—nucleic acids section)

Dr. Harry V. Gelboin (enzyme induction and carcinogen metabolism)

National Heart and Lung Institute
Laboratory of Biochemical Genetics
Dr. Marshall Nirenberg (molecular biology)
Dr. Alan Peterkofsky (nucleic acids and protein synthesis)
Cardiology Branch
Dr. Stephen Epstein (circulatory physiology)
Laboratory of Chemical Pharmacology
Dr. James Gillette (enzymes drug interaction)
Dr. Elwood Titus (drug and transport mechanism)
Dr. Watson D. Reid (drug tissue interaction)
Laboratory of Molecular Diseases
Dr. Martha Vaughan (hormonal control of lipolysis)
Dr. W. French Anderson (protein synthesis and biochemical genetics)
Experimental Therapeutics Branch
Dr. Albert Sjoerdsma (experimental therapeutics)
Dr. Walter Lovenberg (biochemical pharmacology)

National Institute of Allergy and Infectious Diseases
Laboratory of Parasitic Diseases
Dr. Eugene Weinbach (interactions of drugs with mitochondria)

National Institute of Arthritis and Metabolic Diseases
Arthritis and Rheumatism Branch
Dr. Peter Goldman (biochemical pharmacology)
Laboratory of Biochemical Pharmacology
Dr. Herbert Tabor (biochemical pharmacology)
Laboratory of Chemistry
Dr. John W. Daly (biogenic amines and enzymatic hyrdroxylation)
Laboratory of Biochemistry and Metabolism
Dr. Elizabeth Neufeld (genetic disorders of mucopolysaccharide metabolism)

National Institute of Mental Health
Laboratory of Clinical Science
Dr. Julius Axelrod (pharmacology)
Dr. Irwin J. Kopin (medicine)
Laboratory of Cerebral Metabolism
Dr. Louis Sokoloff (cerebral metabolism)
Laboratory of Neuropharmacology
Dr. Floyd E. Bloom (neuropharmacology)
Laboratory of Preclinical Pharmacology
Dr. Erminio Costa (preclinical pharmacology)

Laboratory of Neurochemistry
Dr. Seymour Kaufman (oxygenases; mechanism of actions and interactions)

National Institute of Dental Research
Laboratory of Biological Structure
Dr. Cecil T. G. King (drug-induced malformation)

National Institute of Child Health and Human Development
Laboratory of Biomedical Sciences
Dr. Daniel W. Nebert (molecular pharmacology)

National Institute of Mental Health

John C. Eberhart, Ph. D., Director of Intramural Research

Robert A. Cohen, M.D., Ph. D., Director of Clinical Investigations

This Institute offers an opportunity for post-doctoral research training in psychiatry and in the biological and behavioral sciences. Clinical Associates are assigned clinical responsibility in caring for patients who are admitted for both therapeutic and research purposes. Staff Associates engage in laboratory research in one of the biological or behavioral science laboratories under the preceptorship of one of the senior staff, and may in addition participate in tutorial seminars and other teaching programs, as their needs and desires indicate. After reporting for duty certain Staff Associates who have particular need for and interest in the tutorial seminar program, and whose qualifications are high, may be designated as Research Associates, and will be given priority in admission to the seminar programs.

Most Staff Associate appointments will not involve deferment for residency training under the CORD program. However, an occasional CORD deferment may be available for Staff Associates whose research duties require that they have 1 or more years of residency training.

Lectures, seminars, and group discussion by members of the staff and by visting lecturers complement the training program, making it possible for all Associates to acquire a broad background in the neural and behavioral sciences with more intensive and individualized study in selected aspects of the field.

Descriptions of the NIMH program areas to which Associates will be appointed follow.

The Adult Psychiatry Branch (Lyman C. Wynne, M.D., Ph. D., Chief.* Senior Staff: Dr. W. T. Carpenter, Dr. William Pollin, Dr. David Reiss, Dr. Winfield Scott, Dr. Roger Shapiro, Dr. Helm Stierlin, Dr. John Strauss, Dr. John Zinner) conducts a broad program of psychiatric research, clinical care, specialized clinical training and psychiatric research training. Ordinarily, 2 years of clinical psychiatric residency training should precede arrival on duty; for Clinical Associates, the program is accredited for third-year psychiatric residency training. Candidates for Clinical Associate appointment ordinarily should apply for the year which is 3 years after graduation from medical school (counting 1 year internship and 2 years psychiatric residency).

Associates are appointed to the branch as a whole. However, later on, when coming on duty, the Associate will be assigned to a particular

*Will resign effective July 1, 1972, and Dr. Helm Stierlin will become Acting Chief.

section and senior staff preceptor within the branch, in accord with the nature of branch activities and when possible, the Associate's interests and experience at that date.

The branch is administratively organized into the Office of the Chief and seven sections. In all of these sections which conduct psychiatric treatment, the clinical work emphasizes a psychodynamic approach, especially family psychotherapy with adolescents and their families. Research projects currently include studies of: (1) links between family communication and psychopathology of offspring; (2) adolescent identity crises and their treatment in the family context; (3) genetically identical twins discordant for schizophrenia and their families; (4) criteria for longitudinal predictions and therapy of adolescents and their families; (5) relationships between verbal and perceptual aspects of behavior; (6) assessment and treatment of acute psychotic patients; (7) experimental studies of interaction in families and small groups; and (8) attentional, perceptual, and neurophysiologic variables in schizophrenia and altered states of consciousness.

The Laboratory of Clinical Science (Irwin J. Kopin, M.D., Chief. Senior Staff: Dr. Julius Axelrod, Dr. William E. Bunney, Jr., Dr. Philippe V. Cardon, Dr. Thomas N. Chase, Dr. Frederick K. Goodwin, Dr. Dennis Murphy) conducts a program of research in biochemistry, pharmacology, physiology, medicine and psychiatry and the interrelationships between them. Current research includes: (1) mechanism of action and metabolism of drugs and hormones which act in the nervous system; (2) biochemical studies in endocrine and metabolic disorders of amino acids, catecholamines and other biogenic amines; (3) clinical pharmacology including drug metabolism; (4) circulatory physiology and psychosomatic medicine; (5) longitudinal investigation of patients (acute or episodic psychosis, depression) stressing biological factors (endocrine function, catecholamines, serum proteins, specific enzyme activities; (6) biological rhythms and their control; (7) biological aspects of toxic pyschoses and drug addiction; and (8) relationship of biogenic amines to neurological disorders, including Parkinsonism.

The Laboratory of Neurobiology (Ichiji Tasaki, M.D., Chief) conducts research on the nervous system at several levels ranging from biochemical and biophysical studies of single excitable cells to studies of systems of neurons in the brain. Current research projects include studies on: (1) the excitation process in nerve and muscle membrane using recently developed optical techniques to demonstrate changes in birefringence, turbidity, and fluorescence in excitable tissue during an action potential; (2) biophysics of model membrane systems; and (3) the integration in the brain of visual information and extravisual input (such as eye movements and attention) using single unit recording in awake monkeys performing a learned task.

The Laboratory of General and Comparative Biochemistry (Giulio L. Cantoni, M.D., Chief) conducts investigations on: Mechanisms and pathways of protein biosynthesis; biological methylations; and alkaloid biosynthesis.

The main focus of the laboratory is on the molecular biology of tRNA including determination of the base sequence of purified tRNAs, interaction with messenger RNA and ribosomal particles, biological coding, enzymology of tRNA, physicochemical studies, etc.

The Section on Alkaloid Biosynthesis studies the enzymes involved in alkaloid biosynthesis, their control and biosynthesis in relation to morphogenetic development of the plant; also, enzymatic mechanisms of transmethylation and intermediary metabolism of sulfur-containing amino acids in various conditions.

The Laboratory of Cerebral Metabolism (Louis Sokoloff, M.D., Chief) conducts a program of research on: (1) chemistry of membranes; and mechanism of action of acetylcholine; (2) biochemical and immunochemical studies on myelin; and characterization of CNS proteins and their relationship in autosensitization reactions of the CNS; (3) biochemistry of the developing nervous system; (4) effects of thyroxine and other hormones on protein synthesis and on the development of the nervous system; and (5) regional cerebral blood flow and physiological and environmental factors which influence it during development of the nervous system.

The Laboratory of Neurochemistry (Seymour Kaufman, Ph. D., Chief. Senior Staff: Dr. Howard A. Nash and Dr. David M. Neville, Jr.) conducts investigations in the following areas: (1) the mode of regulation and the mechanism of action of a group of oxidative enzymes called oxygenases. The enzymes currently under study include phenylalanine hydroxylase, tyrosine hydroxylase and dopamine β-hydroxylase; the study includes an investigation at the molecular level of the enzyme defect in phenylketonuria and hyperphenylalaninemia; (2) the biochemical basis for skeletal muscle hypertrophy including the effects of exercise and neural factors in the process; (3) cell surface membrane proteins and their role in cellular differentiation; (4) DNA repair mechanisms and their role in aging; (5) the structure of viral DNA especially in relation to the phenomena of integration of viral DNA into host structures and viral transduction of host genes; (6) electronic structure of DNA and its components with emphasis on specific interactions of nucleotides in cellular processes such as codon-anticodon recognition and DNA replication.

The Laboratory of Neurophysiology (E. V. Evarts, M.D., Chief) conducts research on problems ranging from basic membrane mechanisms to brain and behavior. Current investigations include: (1) physiology and biophysics of membrane; (2) a program on simple nervous systems

such as the *Aplysia;* (3) studies on central nervous system control of movements; (4) neural correlates of learning and memory; and (5) functional role of sleep.

The Laboratory of Psychology (David Rosenthal, Ph. D., Chief) conducts investigations in eight broad research areas: (1) brain function in primates—cortical mechanisms in sensation and perception in the visual auditory and somesthetic systems; cortical mechanisms in problem solving; cortical-subcortical relations in the regulation of behavior; (2) evoked potential and sensori-perceptual studies in humans—exploration of relationships between perceptual response patterns, psychiatric clinical dimensions and neurophysiological measures; (3) etiological studies of schizophrenia with designs to investigate the genetic component of the disease—children of schizophrenics adopted by non-schizophrenic parents are evaluated for psychopathology by using psychological, psychiatric and psychophysiological techniques—comparing biological and adoptive parents of schizophrenic children as they are consecutively admitted to psychiatric facility; (4) developmental and comparative psychology—parametric studies of early learning and motivation in human infancy and childhood; modification of caretaking acts and general environmental conditions and their effects on infant and child behavior; effects of stimulation on behavioral development of infants and children; perceptual development and concept formation without verbal assistance in infants and preschool children; (5) perception, thinking, and problem solving—effects of experimental procedures on time estimation in normals and schizophrenics; ways of increasing efficiency of solving complex cognitive problems; (6) communication—units of syntactic encoding and decoding in conversational speech; frequency of body movements as emotional expression and (7) the creative scientist—the effects of personality, environment and cognitive abilities on creative performance of young as well as mature scientists; longitudinal studies of a potentially creative sample.

The Division of Special Mental Health Research (G. C. Salmoiraghi, M.D., Ph. D., Director), located at Saint Elizabeths Hospital, (1) plans and conducts a program of intramural research on special mental health problems such as psychopharmacology, neuropharmacology, memory, human behavior, and the biochemistry of learning; and (2) performs clinical evaluation and follow-up activities in connection with research patients.

The Laboratory of Clinical Psychopharmacology (Roger K. McDonald, M.D., Chief) conducts research primarily concerned with the mechanism of action of drugs which are relevant to behavior. Within a neurobehavioral frame of reference psychotropic drug actions are evaluated using one or more of the following approaches: neurochemistry, biochemistry, pharmacology, neurophysiology, physiology, animal be-

havior and clinical studies. Associated with the laboratories are extensive animal facilities available for acute and chronic metabolic and behavioral studies. In addition there are two research wards consisting of a 20-bed service and a 16-bed intensive care and study unit. Both patients and normal volunteers are studied in the clinical facilities. Because the Laboratory of Clinical Psychopharmacology consists of both laboratory and clinical research operations, applicants should specify their area of interest.

The Laboratory of Neuropharmacology (F. E. Bloom, M.D., Chief. Senior Staff: Dr. B. J. Hoffer, Dr. G. R. Siggins, Dr. F. F. Weight) conducts a multidisciplinary research program centered upon the identification of synaptic transmitter substances, and the mechanisms by which neuro-active and psycho-active drugs exhibit effects upon synaptic transmission. The approach is entirely at the cellular level, utilizing intracellular and extracellular electrophysiologic techniques, micromethods of drug administration including microelectrophoresis, and cytochemical studies with light, fluorescence and electron microscopy. Specifically, studies are currently being carried out on: (1) the characterization and pharmacology of potential monoamine-containing neuronal pathways in the mammalian central nervous system; (2) the relation between pharmacological responsiveness and development of structurally specialized synapses; and (3) the cytologic and physiologic organization of sympathetic ganglia.

The Laboratory of Preclinical Pharmacology (E. Costa, M.D., Chief) conducts research in neurochemistry and neuropharmacology to elucidate chemical and physicochemical factors involved in the clinical response of drugs affecting neuronal function. The Laboratory is organized into three sections: (1) The Section on Molecular Pharmacodynamics (Dr. E. Costa, Acting Chief. Senior Staff: Dr. I. Hanin and Dr. S. Koslow) conducts studies on: (a) the molecular mechanisms of drug actions in the CNS as they affect the steady-state and the dynamics of neuronal catecholamines, indolealkylamines and acetylcholine; (b) the biochemical mechanisms of drug dependence and habitation; and (c) development of quantitative gas chromatography-mass spectrometry methods to detect drug metabolites, neurotransmitters or their metabolites in isolated neurons. (2) The Section on Biochemical Pharmacology (Dr. N. H. Neff, Acting Chief) conducts investigations directed at measuring turnover rates of enzymes controlling the dynamics of brain neurotransmitters and develops new methods to identify and characterize enzymes controlling formation of polypeptides in brain. (3) The Section on Neuroendocrinology (Dr. B. Weiss, Acting Chief) conducts studies concerned with drug actions on the biochemical controls of neuroendocrinal integration. These studies are focused mainly on interactions of drugs, hormones and transmitters with the adenylate cyclase systems.

National Institute of Neurological Diseases and Stroke

Edward F. MacNichol, Ph. D., Director

General. The National Institute of Neurological Diseases and Stroke conducts, fosters, and coordinates research on the causes, prevention, diagnosis, and treatment of neurological and sensory disorders and related fields, and administers a program of research and training grants and awards.

Throughout the Institute, opportunities also exist for clinical and professional education, including many scientific disciplines.

CORD deferments for approved clinical training beyond a year of internship are available for some Clinical Associate positions in the clinical branches. Research and Staff Associate positions do not provide CORD deferments in this Institute. It is to be noted that Clinical appointments can be made for 2 or 3 years.

Intramural Research Program

Henry G. Wagner, M.D., Director

John M. Van Buren, M.D., Acting Clinical Director

The Medical Neurology Branch (W. King Engel, M.D., Chief) has as its major function the application of basic research techniques to the investigation of clinical neurological problems. The Clinical Associate becomes acquainted with a majority of the neurological diseases, with particular emphasis on the disorders of muscle, myasthenia gravis, lower motor neuron diseases, metabolic abnormalties of the central nervous system, and genetically determined disorders. He receives instruction in clinical neurology and the related clinical and basic sciences while developing an understanding of the various laboratory techniques which support the neurological investigation. During the first 12 months he is in a ward environment and is responsible for the care of patients on the Medical Neurology Service and the integration of related research. He covers the neurologic consultations to the other clinical services during 3 of those months. During the first year he is expected to learn to perform one of a variety of basic laboratory techniques (such as histochemistry, tissue culture, biochemistry, electron microscopy, immunology, or electromyography) as it applies to a clinical problem. The second year

is spent in full-time work on that clinical research technique. Some Clinical Associates may stay a third year to continue their clinical research activities.

The Surgical Neurology Branch (John M. Van Buren, M.D., Acting Chief) is concerned with the investigation of epilepsy, involuntary movements, head injury, developmental disorders, brain tumor, cerebral edema, anatomical effects of surgical lesions on the nervous system, and pyschological assessment of surgical lesions.

The Clinical Associate is required to study and has responsibility for the care of patients with epilepsy, involuntary movements, brain tumors, vascular malformations of the nervous system, and others with a miscellany of neurological disease. He receives practice and instruction in clinical neurology, and, in particular, in the diagnostic techniques of surgical neurology and the operative techniques of neurological surgery as well as the principles on which these techniques are based. He attends clinical rounds in Surgical and Medical Neurology, staff conferences in electroencephalography and X-ray diagnosis, as well as neuropathological conferences. He is advised to acquire as great a familiarity with the various laboratory techniques as is commensurate with his individual responsibilities and the commitments of the various laboratories in the NINDS.

The Electroencephalography Branch (Cosimo Ajmone Marsan, M.D., Chief) involves a relatively small highly specialized patient population from the entire Clinical Center. The position of Clinical Associate is for a 2- or 3-year appointment (preference is given to persons with basic neurological training). In neurophysiology the appointment is also for 2 or 3 years (preference is given to people with some previous experience in the field of electrophysiology and a knowledge of neuroanatomy). Current research: Experimental epilepsy, thalamo-cortical relationship, nature of brain waves, microelectrode study of cortical neurons, etc.

Laboratory of Neurochemistry (Donald B. Tower, M.D., Ph. D., Chief) directs research toward the elucidation of the chemical attributes of neural tissues which underlie the normal functioning of the nervous system and the derangements of function in various neurological diseases. The investigations, which are primarily at the basic level, are distributed among four sections of the laboratory: the Lipid Chemistry Section (Head, Dr. R. O. Brady), the Enzyme Chemistry Section (Head, Dr. R. W. Albers), the Section on Amino Acids and Electrolytes (Head, Dr. D. B. Tower), and Physiology and Metabolism Section (Head, Dr. E. G. Trams). In these investigations a wide variety of disciplinary approaches and methodologies, including appropriate clinical material, are being utilized. Special emphasis is given to the relevance of the various laboratory programs to neurophysiological problems, such as mecha-

nisms subserving reception, conduction and transmission of nerve impulses, and to clinical problems, such as the bases for the lipodystrophies, demyelinating diseases, epilepsy, cerebral edema, and nutritional and genetically-determined disorders.

The Laboratory of Molecular Biology (Ernst Freese, Ph. D., Chief) examines control mechanisms of RNA and membrane synthesis of transport and of differentiation by a combination of genetic and biochemical techniques. Candidates with a M.D. or Ph. D. are accepted.

Bacteria and tissue cultures are used to determine the biochemical reactions involved in transport, RNA control, and differentiation. Mutants are isolated and characterized structurally, by microscopic and electron microscopic techniques, genetically by transduction and transformation, and biochemically, by radioactive measurements, isolation and assays of enzymes, thin-layer and gas chromatography, etc. The biochemical reaction involved in control and development during the commitment period is thus determined.

The Laboratory of Neuropathology and Neuroanatomical Sciences (Igor Klatzo, M.D., Chief) recognizes scientific advantages to be derived from close contact and interaction between various approaches used in the fields of neuropathology and neuroanatomical sciences. Thus investigations on basic pathogenic mechanisms operative in various neuropathological conditions are carried out parallel with or supported by studies elucidating structural and functional features of the normal nervous system. Specific problems under current investigation are: Effects of oxygen deprivation, edema, radiation on the brain, role of the glia, development and pathology of myelin, aspects of vascular permeability and transport mechanisms in the brain, mechanisms of neurohormonal regulation, localization of catecholamines, elucidation of some of the sensory and motor systems, investigation on normal structure and pathologic reactions in a primitive nervous system such as that of the Elasmobranchs. The main technical approaches include light and electron microscopy, histochemistry, radioisotopic, biochemical assays and tissue culture. The Laboratory is divided into eight sections: (1) the Section on Functional Neuroanatomy, (2) the Section on Trophic Nerve Function, (3) the Section on Neurocytology, (4) the Section on Experimental Neuropathology, (5) the Section on Comparative Neuropathology, (6) the Section on Cellular Neuropathology, (7) the Section on Cellular Neurochemistry, and (8) the Section on Neurocytobiology.

The Laboratory of Neurophysiology (M. G. F. Fuortes, M.D., Chief) conducts research on basic properties of nerve cells and on the organization of the nervous system. The *morphology* of cells, synapses and subcellular structures is studied by means of optical and electron microscopy. *Membrane properties* of receptor cells and central neurons are investigated by electrophysiological methods. Studies on *receptor*

functions include analysis of the responses of visual cells to light as well as kinetic studies aimed at determining the properties of the processes leading to the response. The properties of *central neurons and synapses* are studied in simple preparations derived from vertebrates and invertebrates. Electrical and chemical properties of cells in *tissue culture* are also being investigated.

The Laboratory of Experimental Neurology (William F. Caveness, M.D., Chief) includes the following activities: (1) the investigation of the delayed effects of X-irradiation on the visual cortext of the Macaca mulatta utilizing an evoked response from photic stimulation, at successive intervals following exposure. The functional alterations are correlated with alterations in the fine structures of the cortex and subcortical fiber system. Special attention is directed to (a) periodic brain swelling, and (b) retrograde and anterograde transsynaptic degeneration in the visual system; (2) the study of development and propagation of local seizures in the developing brain of the Macaca mulatta with the use of electrophysiological and regional blood flow techniques.

One Associate position is available for 2 to 3 years. Previous experience in electrophysiology or neuroanatomy is essential.

The Laboratory of Neural Control (Karl Frank, Ph. D., Chief) conducts research at applied and basic levels leading to: (1) The development of neural control of external devices, i.e., outward information transfer; through the use of normal and abnormal effector organs; through detection of peripheral motor nerve fiber activity; through detection of activity of other central nervous system neurons. (2) Studies leading to the development of external control of the central nervous system, i.e., inward information transfer; through stimulation of normal and abnormal sensory pathways; through electrodes on sensory nerve pathways; through electrodes in the central nervous system. (3) Research leading to the development of neural modeling for the purpose of studying mechanisms of information processing in the central nervous system.

Applicants for Research or Staff Associate positions in the Laboratory should have special qualifications in neurophysiology, the physical sciences, mathematics, engineering or computer technology. Research experience under the guidance of an established investigator is desirable. The Laboratory of Perinatal Physiology (R. E. Myers, M.D., Ph. D., and staff) functions within the basic neurological disciplines. Areas of specific involvement follow: (1) *Experimental Neuropathology* utilizes biochemical cardiovascular and descriptive neuropathological approaches to explore the patterning and pathogenesis of anoxic brain damage and cerebral palsy. (2) *Physiological Psychology* is concerned with the identification and characterization of neural mechanisms underlying such psychological functions as perception, memory and learning.

(3) *Experimental Social Behavior*—Investigates experimental and neural bases of primate social and instinctual behavior. (4) *Developmental Neurology*—The dated monkey pregnancy program within the Laboratory enables studies within the broad area of development utilizing techniques of morphology, physiology or biochemistry.

The Laboratory of Biophysics (William J. Adelman, Jr., Ph. D., Chief) carries on an active research program in experimental, analytical, and theoretical biophysics. This program is concerned with uncovering the basic mechanisms underlying excitation, conduction and transmission of the nerve impulse. A number of approaches are used to reach this goal.

The first involves studying the excitable membranes of single giant axons from *Loligo* and *Myxicola,* and the synaptic processes in the *Loligo* giant synapse. These neural membrane systems are compared with the membranes of giant muscle fibers such as are found in *Balanus nubilus*. These studies involve the voltage clamp technique, internal perfusion of fibers with artificial media replacing the intracellular cytoplasm, as well as other physical techniques such as electron paramagnetic resonance (EPR) of spin labeled probes, and photon emission of fluorescent probes incorporated into excitable membrane components.

The second approach involves the study of artificial bilayer membranes so as to elucidate basic chemical and physical mechanisms for the voltage and time dependencies for ionic permeabilities of excitable membranes. In this connection the voltage clamp, EPR and fluorescence techniques are utilized.

Thirdly, the Laboratory supports a powerful mathematical program so as to provide modern data reduction approaches as well as theoretical models of excitable membrane systems. This program makes use of the newest techniques in computer science.

Collaborative and Field Research Program

Warren V. Huber, M.D., Associate Director

The major activities of scientists in the Collaborative and Field Research Program are in planning and carrying out organized or targeted research programs, particularly in such areas as head injury, epilepsy and neurologic disorders of childhood. In addition, epidemiologic, genetic, and biostatistical studies investigating the causes and contingent factors affecting the rates of various neurological disorders, including impairment or malfunctioning of sensory disorders, are pursued.

The Central Nervous Systems Studies Branch, under the direction of Dr. D. Carleton Gajdusek, is engaged in studies of child growth and development, and slow, latent, and temperate virus infections of the central nervous system. Much of the program derives from the study of

the disease kuru and Jakob-Creutzfeldt disease, and similar subacute degenerative disorders which have successfully been transmitted to the chimpanzee and other non-human primates. The child growth study involves all aspects of the cultural and physical anthropology of native people in relation to their environment, as well as repeated medical, genetic, and microbiological examination of these intensely studied groups. Special research films are prepared on many aspects of these primitive peoples.

The Applied Neurologic Research Branch, under Dr. J. Kiffin Penry, is composed of the Sections on Head Injury and on Epilepsy.

The Section on Head Injury is presently engaged in a collaborative study of the criteria of cerebral death and is attempting to verify or modify current clinical and electroencephalographic criteria in relation to patient age and cause of coma. Patients who have recovered after having fulfilled the criteria for presumed cerebral death will be assessed for neurological deficit. The Section will be involved in proposed future head injury programs.

The Section on Epilepsy is concentrating its effort on controlled clinical studies for the evaluation of experimental anticonvulsant drugs. This Section is also deeply involved in coordinating and conducting collaborative studies of epilepsy in order to identify the consequences associated with, or developing from, this disorder; evaluating the means and the extent to which the course of the disease can be altered; investigations of the role of etiologic factors; and research to improve diagnostic and therapeutic techniques.

The Epidemiology Branch, under Dr. Jacob A. Brody, has laboratory facilities and a Section on Genetics in Epidemiology in Bethesda, Maryland, and a research center in Guam. Diseases being studied epidemiologically includes multiple sclerosis, neurological syndromes and lung cancer, measles and subsequent neurological and psychological abnormalities, and amyotrophic lateral sclerosis. Major efforts in genetics have been studies of dystonia musculorum deformans and accoustic neuroma. Amyotrophic lateral sclerosis and Parkinsonism Dementia are being intensively studied on Guam, both clinically and in their epidemiologic, genetic and neuropathologic patterns.

The Infectious Diseases Branch, under Dr. John L. Sever, develops and utilizes large-scale serological methods to study the relation between viral, protozoal, and bacterial infections, and birth defects and related abnormalities; conducts investigations on microorganisms to produce antisera to these agents and to determine the effects of these microorganisms on animal and fetal tissues; and investigations in the recovery of infectious agents and chromosome changes in fetal tissue specimens.

The Perinatal Research Branch. For several years this branch has been conducting a program of research concerned with the correlation of factors operating in pregnancy to cerebral palsy, mental retardation and other neurological and sensory disorders of infancy and childhood. Presently subject area task forces, in collaboration with an overall advisory committee, are guiding staff effort and attention to statistical analysis to identify major trends, developmental patterns, and risk factors.

Division of Biologics Standards

Roderick Murray, M.D., Director

The Division of Biologics Standards is accepting applications for Staff Associateships in the Laboratory of Bacterial Products, Laboratory of Pathology, Laboratory of Viral Immunology, and Laboratory of Virology and Rickettsiology. Appointments are for a 2-year period beginning each July 1, depending on the ability of the laboratories to accept candidates at each time and on the candidates' desires for deferment.

The Laboratory of Bacterial Products (Harold Baer, Ph. D., Chief) is engaged in a program of basic and applied research in immunology and microbiology as related to bacterial vaccines, mycoplasmas, toxins, allergens, and mycobacterial and fungal antigens. Studies are being carried out in a number of areas, including: delayed hypersensitivity and tolerance; immunological mechanisms of infection and immunity utilizing whole bacterial vaccines as well as purified and characterized antigens; measurement of the kind of antibody response. Programs will attempt to take advantage of the interest and prior experience of the applicant.

The Laboratory of Pathology (Ruth L. Kirschstein, M.D., Chief) is engaged in a program of research in the pathogenesis of infectious diseases, hypersensitivity and immunologic responses with special emphasis on oncogenic viruses and those infectious agents for which there are vaccines and/or other methods of prevention. Animal models of infectious diseases or tumor-producing systems are studied as to the mode of transmission within the colony, spread within each animal, and the final pathologic changes that occur.

Staff Associates will receive extensive training in the pathology of various infectious diseases and animal tumors using the wealth of material accumulated in the last 10 years. In addition, there are opportunities to develop individual research projects in the area of infectious diseases and oncogenesis. Persons interested in such an assignment should have a broad interest in medicine and/or pathology.

The Laboratory of Viral Immunology (Harry M. Meyer, Jr., M.D., Chief) and the Laboratory of Virology and Rickettsiology (Nicola Tauraso, M.D., Chief) are engaged in programs of virus research with special emphasis on the study of viruses of current or potential importance in the biologics field. Although each laboratory participates in clinical trials of vaccines on occasion, individuals should anticipate spending all or most of their time in laboratory research. Each Staff Associate works under the guidance of a senior member of the professional staff. Projects vary from basic to applied research depending

on the interests of the individual and the needs of the Division. Assignment to these laboratories offers the opportunity to acquire a foundation in laboratory virology and for this reason would be most valuable to physicians planning academic careers in infectious diseases or related fields. The above laboratories give preference to applicants with 1 or more years of residency training in pediatrics or medicine, but do not require prior experience in virology.

The Clinical Center

Thomas C. Chalmers, M.D., Director

Roger L. Black, M.D., Associate Director

Jerome B. Block, M.D., Associate Director

The Clinical Center appoints Clinical Associates for the Departments of Anesthesiology, Diagnostic Radiology, Blood Bank, Clinical Pathology, and Nuclear Medicine. Associates in Anesthesiology and Diagnostic Radiology are expected to have completed their residencies prior to entrance on duty.

The Anesthesiology Department (Clarence L. Hebert, M.D., Chief) offers advanced training—through the Associate program—to medical graduates who have fulfilled residency requirements of the American Board of Anesthesiology, and who have special interest in research. (Senior residents from other hospitals are accepted for brief periods for special training. Arrangements for such assignments must be made well in advance by the director of the residency program.)

The Anesthesiology Department is organized as a central service to provide anesthesiological care for all patients hospitalized at the Clinical Center, NIH. Inhalation therapy and consultative service for special problems (respiratory, pain, etc.) are included.

Three of the National Institutes of Health have surgical services which have active programs in surgical research.

The National Cancer Institute (Surgery Branch) has a long-range program concerned with the performance of extensive radical surgery with special emphasis on the treatment of patients with malignancy of pelvic organs and structures of the head and neck. In addition, various types of other general surgery are done on NCI patients and those patients sponsored by other Institutes, who require surgery during their Clinical Center stay.

The National Heart Institute admits patients for the study and treatment of congenital and acquired heart disease. All types of cardiac surgery are performed, the majority consisting of open-heart operations performed with the aid of extracorporeal circulation. Six or more of these operations are done weekly.

The National Institute of Neurological Diseases and Stroke has several surgical programs including: localization and surgical removal of epileptogenic foci within the temporal lobe for the treatment of epilepsy; sterotaxic producedues for the relief of syndromes characterized abnormal movements and rigidity; and the removal of malignant lesions of the brain.

The Blood Bank Department (Paul J. Schmidt, M.D., Chief) is accepting applications for Clinical Associateships under the matching system.

The Department supplies over 20,000 blood products annually for transfusion to patients with unique hematologic and immunologic problems. Competent therapy is stressed and clinical programs involving the major blood components are in progress. The medical staff consists of three full-time staff physicians, and two Clinical Associates, as well as residents and medical students who are there for varying periods of training.

In addition to its service function, a significant proportion of Blood Bank activity is oriented toward clinical and basic research. As a focal point in patient care and as a repository of diverse blood samples, the Blood Bank provides a unique opportunity for collaborative research with the various Institutes. Current programs include investigations into hepatitis and the hepatitis associated (Australia) antigen, the effects of biologic incompatibilities on transfusion and transplantation, immunologic studies of drug-induced hemolytic anemias, and the use of computers in laboratory medicine.

The program offers training for the clinician in the laboratory management of a patient-oriented transfusion program as well as advanced training for the clinical pathologist. A close professional liaison is maintained with the Clinical Pathology Department.

The Clinical Pathology Department (Jerome B. Block, M.D., Acting Chief) is accepting applications for Clinical Associates whose interests lie in specialized training and research in laboratory medicine. The Department is organized into four main sections: Clinical Chemistry, Hematology, Microbiology, and Research, Development and Laboratory Automation. These areas are staffed by over 100 professional and technical personnel who form the operational base for the broad spectrum of laboratory diagnostic services called upon by the various Institutes for their intramural patient care programs. In addition, the professional staff of the Department is engaged in collaborative and independent research in the areas relevant to laboratory medicine and the clinical diagnostic problems encountered at the Clinical Center. The Department participates in the training of Residents in Clinical Pathology and interacts fully and on a professional consultative basis with the clinical programs at the National Institutes of Health.

Among the procedures and programs currently in operation in the Department are automated assay systems for laboratory diagnosis, carbohydrate chromotography, amino-acid analysis, gas chromotography, radio-immuno assays, tissue culture, coagulation factor studies, and new approaches in the interface between computer assisted laboratory automation and data processing. These latter programs, in particular, are facilitated by direct access to the Department's own computer facilities.

The program for Clinical Associates is of two years duration with potential for subsequent entrance into the Residency Training Program in Clinical Pathology.

The Department of Diagnostic Radiology (Betty E. Hathaway, M.D., Chief) offers a 2-year Clinical Associate program of experience in all phases of diagnostic radiology and advanced training in special study procedures which include: Angiocardiography; femoral ateriography; selective celiac and renal ateriography; inferior venocavography; lymphangiography; carotid and vertebral ateriography; bronchial arteriography; pneumoencephalography and ventriculography; retroperitoneal air studies; sialography; and gynecography.

The Department provides complete diagnostic X-ray services for all of the patients in the Clinical Center. The clinical material studied radiographically is most unusual and many opportunities are available for clinical research.

Approximately 45,000 X-ray examinations are performed annually on 26,500 patients including 2,000 special study procedures.

The Department staff is composed of 10-full-time radiologists, 19 X-ray technicians, 2 nurses, and 16 accessory personnel.

The professional and physical environment is excellent and close liaison is maintained with the Radiation Therapy Department, the Department of Nuclear Medicine, and the radiology departments of all local hospitals.

The Department of Nuclear Medicine (Gerald S. Johnston, M.D., Chief). One Clinical Associate is accepted each year for a 2-year training period. Preference will be given to applicants with training in Nuclear Medicine. The specific field of previous residency training is not a primary consideration, but 1 year in approved Internal Medicine, Radiology, or Clinical Pathology is recommended in order to meet the requirements for certification in Nuclear Medicine.

The Department consists of three sections: Diagnostic Nuclear Medicine Section, Whole Body Counter Section, and Radiation Safety Section.

Radiopharmaceutical service is provided by the Pharmacy Department. There are three full-time radiopharmacists who are available for consultation and provide support for the Department of Nuclear Medicine in its employment of radiopharmaceuticals for diagnostic and investigative purposes.

The Diagnostic Nuclear Medicine Section provides diagnostic and investigative service to the physicians of the various Institutes working within the Clinical Center. Dual probe rectilinear scanners and gamma cameras are the basic imaging devices. Computer support is available within the Section. The Whole Body Counter Section works closely with the Diagnostic Section and the Radiation Safety Section. It operates three whole body counters and provides a consultation service to all the Institutes. It is engaged in basic research on trace quantities of radio-

activity, personnel monitoring, and a variety of clinical studies. The staff of the Whole Body Counter and Diagnostic Sections consists of five physicians, a radiobiologist, a nuclear physicist, an equipment specialist, and six nuclear medical technicians.

The Radiation Safety Section provides a variety of services including the assay of all radionuclides for human use. Other responsibilities include accounting for the 80 curies of radionuclides received and disposed of each year at NIH, performing calibration and safety checks on the 125 X-ray producing machines and 300 sealed sources, and evaluating over 12,000 film-monitoring badges a year. There are 10 health physicists working within the Radiation Safety Section who assist personnel working with sources of radiation throughout the NIH.

PART FOUR

Academic Programs Available to Associates

AMONG the academic programs open to an NIH Associate are: Evening courses provided by the Foundation for Advanced Education in the Sciences, Inc.; formal Seminars under the direction of NIH staff; Combined Clinical Staff Conferences; formal lectures; symposia; and an annual scientific equipment exhibit. The "N.I.H. Calendar of Events" lists an average of 15 to 25 programs each week. Other events of interest are held at universities and other institutions in the Washington-Baltimore area.

Evening Courses

Evening courses are provided by The Graduate Program of the Foundation for Advanced Education in the Sciences, Inc. Established by scientists who subscribe to the view that learning, research, and teaching are mutually reinforcing processes essential to the evolution of science, the Foundation is a non-Federal independent organization as defined by the Government Employees Training Act; however, its tuition and other fees can be paid by a Federal employer. Courses are offered in two semesters, fall and spring; courses are offered at the undergraduate and graduate levels under the programs of its several Departments of instruction: Behavioral and social sciences, biochemistry, chemistry, genetics, mathematics, statistics, physics, medicine and physiology, microbiology and immunology, languages and general studies. Further inquiries regarding The Graduate Program and requests for its current catalog should be directed to: Registrar, The Graduate Program, Foundation for Advanced Education in the Sciences, Inc., National Institutes of Health Bethesda, Md. 20014.

Seminars

An NIH Program of formal tutorial seminars and informal discussion groups is designed in content and emphasis for prospective independent investigators, and gives them the additional opportunity to master selected topics not adequately covered during college or graduate school-

ing. These exercises are an integral part of the Associate Program and are geared specifically in that direction. The program accommodates Research, Staff, and Clinical Associates and other properly qualified persons.

A number of tutorial seminars are generally made available each academic year in each of the following categories: biochemistry and genetics; mathematics and physical chemistry; cell biology, immunology and physiology.

Weekly seminars run from September through January and from February through June. Each session is of 2 to 3 hours' duration, and the participants present specific material under the direction of a qualified expert in the field. In preparation for these, the Associate does appropriate outside reading.

Combined Clinical Staff Conferences and Lectureships

Aside from the rounds and staff conferences within the separate Institutes engaged in clinical research, the Clinical Center sponsors at least one monthly Combined Clinical Staff Conference for 9 months of the year. Each conference is conducted by one of the Institute services or an appropriate Department of the Clinical Center. This series of conferences is complemented by Grand Rounds which, in effect, serves the same purpose. The conferences—open to the entire clinical staff and those engaged in laboratory research as well—center around clinical case material having interest for a large portion of the staff, and serve to keep individual investigators abreast of current emphasis in all clinical research.

Several formal lectures are presented annually. The National Institutes of Health Lecture Series was established in 1953 to recognize outstanding scientific accomplishment and to contribute to the interchange of scientific information. The lectureships are awarded by the Director of NIH on the advice of the Scientific Directors of the Institutes. The R. E. Dyer Lectureship was established in 1950 by friends and colleagues of Dr. Rolla E. Dyer, Director of the National Institutes of Health, 1942–50, to pay him tribute upon the occasion of his retirement from the Public Health Service. The award is made at appropriate times—usually on an annual basis—to a scientist who has made an outstanding contribution to knowledge in a field of medical science; and is administered by NIH.

The Jules Freund lecture series was established in 1961 and is presented annually in honor of the first Chief of the Laboratory of Immunology, National Institute of Allergy and Infectious Diseases.

The G. Burroughs Mider Lectureship was established in 1968 by the Scientific Directors to honor Dr. Mider for his distinguished service to NIH. On advice of the Scientific Directors, these lectureships are

awarded annually by the Director, NIH, to a scientist who has contributed significantly to the biomedical research eminence of NIH.

Equipment Exhibit: Symposia

The NIH Research Equipment Exhibit was established in 1951 to acquaint scientists with the most modern research tools and to give them an opportunity to discuss equipment problems with representatives of industry. In 1954, a Symposium on Recent Developments in Research Methods and Instrumentation was added, offering a balanced presentation by specialists in many areas of biomedical research. The two annual events combined to provide a convenient setting for the exchange of information between research investigators and manufacturers of scientific equipment.

The NIH International Symposium on Biomedical Research was established in 1963 to emphasize the mutuality of interest of NIH and the international scientific community, particularly with the extension of NIH programs overseas.

The Washington-Baltimore Educational Complex

The Washington-Baltimore area is widely known for its educational advantages. For example, three medical schools (Howard, Georgetown, and George Washington) are located in the District of Columbia and two (Johns Hopkins and the University of Maryland) are in Baltimore. These and the universities with which they are associated, together with unique institutions such as the Armed Forces Institute of Pathology and the Naval Medical Center, offer exceptional opportunities. Some Associates find the time to pursue a certain amount of formal education at such nearby institutions.

Library Facilities

The National Institutes of Health Library (located in the Clinical Center) provides a central facility for all scientists, technicians, administrators, and supporting staff who are engaged in the research program. As a self-service, open-stack library, it contains a collection of 110,000 volumes and receives 5,000 monographs and 3,000 foreign and domestic journals. Its translation service and the proficiency of its staff in compiling bibliographies are noteworthy.

The National Library of Medicine is located on the NIH campus. While this library serves the entire country, its proximity makes it especially valuable to NIH investigators. Holdings exceed 1 million items —books, journals, theses, pamphlets, prints, and microfilm. Researchers may consult material at the Library and may request printed material through the NIH interlibrary loan service.

Addendum

Clinical Electives for Medical Students

The National Institutes of Health conducts a program of elective courses open to students from any of the nation's medical schools. For 1972–1973, the staffs of several Institutes are collaborating to supply an in-depth exposure to three clinical sub-specialties: Endocrinology, Hematology, and Immunology, and the biomedical uses of computers.

The essence of this educational experience is a close association between the student, clinical associates, and physician-scientists in several of the Institutes.

Students have patients assigned to them for workup, discussion, and participation in the pertinent studies. Special rounds and conferences are held with students. Also, students are encouraged to take part in all regular clinical and research conferences, and journal clubs.

Requests for a descriptive catalog and information concerning application for a clinical specialty elective should be addressed to:

Thomas C. Chalmers, M.D.
Director, Clinical Center, and
Chairman, Committee on Specialty Electives
National Institutes of Health
Bethesda, Md. 20014

Residency Programs

Fully approved residency programs are offered in clinical pathology, anatomical pathology, combined clinical and anatomical pathology, and oral pathology and dental public health. Requests for information and application forms regarding these programs should be addressed to the respective program chiefs:

Jerome B. Block, M.D.
Acting Chief, Clinical Pathology Department
Clinical Center
National Institutes of Health
Bethesda, Md. 20014

Louis B. Thomas, M.D.
Chief, Laboratory of Pathology
National Cancer Institute
National Institutes of Health
Bethesda, Md. 20014

Howell O. Archard, D.D.S.
Chief, Diagnostic Pathology
National Institute of Dental Research
National Institutes of Health
Bethesda, Md. 20014

Harold Englander, D.D.S., M.P.H.
Chief, Clinical Trials Section
National Institute of Dental Research
National Institutes of Health
Bethesda, Md. 20014

On the basis of agreements between program chiefs and appropriate American Specialty Boards, Clinical Associates in dermatology, psychiatry, and neurology may receive credit for 1 year each. Associates in internal medicine who remain at NIH for a third year may receive credit for this year upon application to the American Board of Internal Medicine.

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